WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Monday, March 29, 2004

Hide?	Set Name	Query	Hit Count
		DB=PGPB; PLUR=YES; OP=AND	
☐	L14	((type 5 or type 8) same polysaccharide$ same (conjugate$ or glycoconjugate$)) and staphylococc$	15
☐	L13	(type 5 or type 8) and polysaccharide$ and (conjugate$ or glycoconjugate$) and staphylococc$	1229
☐	L12	type and (5 or 8) and polysaccharide$ and (conjugate$ or glycoconjugate$) and staphylococc$	1229
☐	L11	L10	0
		DB=DWPI; PLUR=YES; OP=AND	
☐	L10	type and (5 or 8) and polysaccharide$ and (conjugate$ or glycoconjugate$) and staphylococc$	7
		DB=EPAB; PLUR=YES; OP=AND	
☐	L9	type and (5 or 8) and polysaccharide$ and (conjugate$ or glycoconjugate$) and staphylococc$	0
☐	L8	L5	0
☐	L7	L6	0
		DB=PGPB; PLUR=YES; OP=AND	
☐	L6	L5	0
		DB=USPT; PLUR=YES; OP=AND	
☐	L5	L3 and (immunocomprom$ or renal or elderly or neonate or surgery or immunosuppress$)	468
☐	L4	L3 and (immunocomprom$ or renal or elderly or neonate or surgery or immunosuppress$)	468
☐	L3	type and (5 or 8) and polysaccharide$ and (conjugate$ or glycoconjugate$) and staphylococc$	1111
☐	L2	L1 same staphylococc$	20
☐	L1	type same (5 or 8) same polysaccharide$ same (conjugate$ or glycoconjugate$)	111

```
$%^Dialog;HighlightOn=%%%;HighlightOff=%%%;

Logging in to Dialog

Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ********
ENTER PASSWORD:
 ********
Welcome to DIALOG

Dialog level 04.01.00D

Last logoff:  20mar04 17:13:42
Logon file405 29mar04 09:06:42
           *** ANNOUNCEMENT ***
                    ***
--File 654 - US published applications from March 15, 2001 to the
present are now online.  Please see HELP NEWS 654 for details.

                    ***
--File 581 - The 2003 annual reload of Population Demographics is
complete. Please see Help News581 for details.

                    ***
--File 990 - NewsRoom now contains February 2003 to current records.
File 992 - NewsRoom 2003 archive has been newly created and contains
records from January 2003. The oldest months's records roll out of
File 990 and into File 992 on the first weekend of each month.
To search all 2003 records BEGIN 990, 992, or B NEWS2003, a new
OneSearch category.
                    ***
--Connect Time joins DialUnits as pricing options on Dialog.
See HELP CONNECT for information.
                    ***
                    ***
--SourceOne patents are now delivered to your email inbox
as PDF replacing TIFF delivery. See HELP SOURCE1 for more
information.
                    ***
--Important news for public and academic
libraries.  See HELP LIBRARY for more information.
                    ***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
                    ***
NEW FILES RELEASED
***DIOGENES: Adverse Drug Events Database (File 181)
***World News Connection (File 985)
***Dialog NewsRoom - 2003 Archive (File 992)
***TRADEMARKSCAN-Czech Republic (File 680)
***TRADEMARKSCAN-Hungary (File 681)
***TRADEMARKSCAN-Poland  (File 682)
                    ***
UPDATING RESUMED
```

```
                    ***
RELOADED
***Medline (Files 154-155)
***Population Demographics -(File 581)
***CLAIMS Citation (Files 220-222)

REMOVED
                    ***

      >>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
      >>>    of new databases, price changes, etc.      <<<
                    ****
*
*
* ALL NEW CURRENT YEAR RANGES HAVE BEEN * * *
* * * INSTALLED   * * *
SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.9 term=ASCII
                      *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

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      /H = Help            /L = Logoff          /NOMENU = Command Mode


Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
? dialog
>>Invalid Option Number

                      *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

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```

```
      /H = Help            /L = Logoff          /NOMENU = Command Mode

Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
? b 410

       29mar04 09:06:44 User226352 Session D758.1
            $0.00    0.167 DialUnits FileHomeBase
     $0.00  Estimated cost FileHomeBase
     $0.00  Estimated cost this search
     $0.00  Estimated total session cost   0.167 DialUnits

File 410:Chronolog(R)  1981-2004/Apr
       (c) 2004 The Dialog Corporation

      Set  Items  Description
      ---  -----  -----------
? set hi %%%;set hi %%%
HILIGHT set on as '%%%'%%%
%%%HILIGHT set on as '%%%'
? b medicine
       29mar04 09:06:58 User226352 Session D758.2
            $0.00    0.074 DialUnits File410
     $0.00  Estimated cost File410
     $0.05  TELNET
     $0.05  Estimated cost this search
     $0.05  Estimated total session cost   0.242 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R)  1969-2004/Mar W3
         (c) 2004 BIOSIS
  File  34:SciSearch(R) Cited Ref Sci  1990-2004/Mar W3
         (c) 2004 Inst for Sci Info
  File  35:Dissertation Abs Online  1861-2004/Feb
         (c) 2004 ProQuest Info&Learning
  File  48:SPORTDiscus  1962-2004/Mar
         (c) 2004 Sport Information Resource Centre
  File  65:Inside Conferences  1993-2004/Mar W3
         (c) 2004 BLDSC all rts. reserv.
  File  71:ELSEVIER BIOBASE  1994-2004/Mar W2
         (c) 2004  Elsevier Science B.V.
  File  73:EMBASE  1974-2004/Mar W3
         (c) 2004 Elsevier Science B.V.
  File  91:MANTIS(TM)  1880-2003/Aug
         2001 (c) Action Potential
  File  94:JICST-EPlus  1985-2004/Mar W2
         (c)2004 Japan Science and Tech Corp(JST)
  File  98:General Sci Abs/Full-Text  1984-2004/Feb
         (c) 2004 The HW Wilson Co.
  File 135:NewsRx Weekly Reports  1995-2004/Mar W3
         (c) 2004 NewsRx
*File 135: New newsletters are now added. See Help News135 for the
complete list of newsletters.
  File 144:Pascal  1973-2004/Mar W3
         (c) 2004 INIST/CNRS
```

```
  File 149:TGG Health&Wellness DB(SM)  1976-2004/Mar W3
        (c) 2004 The Gale Group
  File 155:MEDLINE(R)  1966-2004/Mar W3
        (c) format only 2004 The Dialog Corp.
*File 155: Medline has been reloaded. Accession numbers
have changed. Please see HELP NEWS 154 for details.
  File 156:ToxFile  1965-2004/Mar W4
        (c) format only 2004 The Dialog Corporation
  File 159:Cancerlit  1975-2002/Oct
        (c) format only 2002 Dialog Corporation
*File 159: Cancerlit ceases updating with immediate effect.
Please see HELP NEWS.
  File 162:Global Health  1983-2004/Feb
        (c) 2004 CAB International
  File 164:Allied & Complementary Medicine  1984-2004/Mar
        (c) 2004 BLHCIS
  File 172:EMBASE Alert  2004/Mar W3
        (c) 2004 Elsevier Science B.V.
  File 266:FEDRIP  2004/Feb
        Comp & dist by NTIS, Intl Copyright All Rights Res
  File 369:New Scientist  1994-2004/Mar W3
        (c) 2004 Reed Business Information Ltd.
  File 370:Science  1996-1999/Jul W3
        (c) 1999 AAAS
*File 370: This file is closed (no updates). Use File 47 for more current
information.
  File 399:CA SEARCH(R)  1967-2004/UD=14014
        (c) 2004 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
Alert feature enhanced for multiple files, etc. See HELP ALERT.
  File 434:SciSearch(R) Cited Ref Sci  1974-1989/Dec
        (c) 1998 Inst for Sci Info
  File 444:New England Journal of Med.  1985-2004/Mar W4
        (c) 2004 Mass. Med. Soc.
  File 467:ExtraMED(tm)  2000/Dec
        (c) 2001 Informania Ltd.
*File 467: For information about updating status please see Help News467.

      Set  Items  Description
      ---  -----  -----------
? s type(w)5 or type(w)8 and Staphylococc?
<------User Break------>
u!
? s (type(w)5 or type(w)8) and Staphylococc?
Processing
Processed  10 of  26 files ...
Processing
Processed  20 of  26 files ...
Processing
Completed processing all files
        5629469  TYPE
       12892540  5
          19534  TYPE(W)5
        5629469  TYPE
        6681934  8
           4257  TYPE(W)8
         426182  STAPHYLOCOCC?
```

```
      S1      762  (TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
? rd s1
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...examined 50 records  (300)
...examined 50 records  (350)
...examined 50 records  (400)
...examined 50 records  (450)
...examined 50 records  (500)
...examined 50 records  (550)
...examined 50 records  (600)
...examined 50 records  (650)
>>>Record 266:210270 ignored; incomplete bibliographic data, not retained -
in RD set
...examined 50 records  (700)
...examined 50 records  (750)
...completed examining records
      S2      295  RD S1 (unique items)
? s staphylococc? and vaccin? and polysaccharide?
          426182  STAPHYLOCOCC?
          746152  VACCIN?
          311057  POLYSACCHARIDE?
      S3      680  STAPHYLOCOCC? AND VACCIN? AND POLYSACCHARIDE?
? rd s3
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...examined 50 records  (300)
...examined 50 records  (350)
...examined 50 records  (400)
...examined 50 records  (450)
...examined 50 records  (500)
>>>Record 266:210270 ignored; incomplete bibliographic data, not retained -
in RD set
>>>Record 266:210268 ignored; incomplete bibliographic data, not retained -
in RD set
...examined 50 records  (550)
...examined 50 records  (600)
...examined 50 records  (650)
...completed examining records
      S4      452  RD S3 (unique items)
? ds.

Set     Items   Description
S1        762   (TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
S2        295   RD S1 (unique items)
S3        680   STAPHYLOCOCC? AND VACCIN? AND POLYSACCHARIDE?
S4        452   RD S3 (unique items)
? s4 and (immunocomprom? or renal or hemodialysis or immunosuppress? or AIDS or
diabetic or neonates or elderly or transplant or surical or burn)
Processing
Processed  10 of  26 files ...
```

```
Processing
Processed  20 of  26 files ...
Completed processing all files
        12560743  4
           75588  IMMUNOCOMPROM?
         1633805  RENAL
          207169  HEMODIALYSIS
          514370  IMMUNOSUPPRESS?
          645032  AIDS
          527969  DIABETIC
          138662  NEONATES
          662383  ELDERLY
          367722  TRANSPLANT
              14  SURICAL
          119797  BURN
      S5  833359  4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR
                  IMMUNOSUPPRESS? OR AIDS OR DIABETIC OR NEONATES OR
                  ELDERLY OR TRANSPLANT OR SURICAL OR BURN)
? s s4 and (immunocomprom? or renal or hemodialysis or immunosuppress? or AIDS
or diabetic or neonates or elderly or transplant or surical or burn)
             452  S4
           75588  IMMUNOCOMPROM?
         1633805  RENAL
          207169  HEMODIALYSIS
          514370  IMMUNOSUPPRESS?
          645032  AIDS
          527969  DIABETIC
          138662  NEONATES
          662383  ELDERLY
          367722  TRANSPLANT
              14  SURICAL
          119797  BURN
      S6      140  S4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR
                  IMMUNOSUPPRESS? OR AIDS OR DIABETIC OR NEONATES OR
                  ELDERLY OR TRANSPLANT OR SURICAL OR BURN)
? rd s6
...examined 50 records  (50)
...examined 50 records  (100)
...completed examining records
      S7      140  RD S6 (unique items)
? ds

Set     Items   Description
S1        762   (TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
S2        295   RD S1 (unique items)
S3        680   STAPHYLOCOCC? AND VACCIN? AND POLYSACCHARIDE?
S4        452   RD S3 (unique items)
S5     833359   4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOSU-
             PPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSPL-
             ANT OR SURICAL OR BURN)
S6        140   S4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOS-
             UPPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSP-
             LANT OR SURICAL OR BURN)
S7        140   RD S6 (unique items)
? t s7/7/1-5

 7/7/1      (Item 1 from file: 5)
```

DIALOG(R)File 5:Biosis Previews(R)

0014778346 BIOSIS NO.: 200400145007
Development of StaphVAXTM, a %%%polysaccharide%%% conjugate %%%vaccine%%% against S. aureus infection: From the lab bench to phase III clinical trials.
AUTHOR: Fattom Ali I (Reprint); Horwith Gary; Fuller Steve; Propst Myra; Naso Robert
AUTHOR ADDRESS: NABI Biopharmaceuticals, 12280 Wilkins Avenue, Rockville, MD, 20852, USA**USA
AUTHOR E-MAIL ADDRESS: afattom@nabi.com
JOURNAL: Vaccine 22 (7): p880-887 17 February, 2004 2004
MEDIUM: print
ISSN: 0264-410X _(ISSN print)
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Staphylococcus%%% aureus is the most common nosocomial pathogen and is responsible for approximately one-third of hospital-acquired bacteremias. The emergence of strains with multidrug resistance, including resistance to vancomycin, the antibiotic of last resort, presents the medical community with a major public health problem. Alternative therapies, including immunotherapy, have been in development for several decades. The discovery of S. aureus capsular %%%polysaccharides%%% from clinical isolates, and their importance to pathogenicity via antiphagocytic activity, opened a new window of opportunity for development of %%%vaccines%%% and immunotherapy against this pathogen. A conjugate %%%vaccine%%%, StaphVAXTM that includes the two most prevalent capsular %%%polysaccharides%%%, types 5 and 8, coupled to a carrier protein efficient in promoting a Th2 response, was developed. In a recent phase III clinical study in %%%hemodialysis%%% patients, StaphVAXTM was shown to prevent S. aureus bacteremia for up to 10 months following a single immunization. The history, epidemiology, serology, and development of StaphVAXTM, including preclinical and clinical studies demonstrating efficacy are described in this review.

7/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014388995 BIOSIS NO.: 200300347714
In vivo production of capsular %%%polysaccharide%%% (CP) production as evidenced by type specific antibody increase following %%%Staphylococcus%%% aureus (SA) bacteremia in %%%hemodialysis%%% patients.
AUTHOR: Fattom A I (Reprint); Wu Y (Reprint); Propst M (Reprint); Fuller S (Reprint); Horwith G (Reprint); Naso R (Reprint)
AUTHOR ADDRESS: Nabi Biopharmaceuticals, Rockville, MD, USA**USA
JOURNAL: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy 42 p238 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy San Diego, CA, USA September 27-30, 2002; 20020927
SPONSOR: American Society for Microbiology

DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: StaphVAX(R), a conjugate %%%vaccine%%% containing types 5 and 8 SA CP, demonstrated significant protection against SA bacteremia in %%%hemodialysis%%% patients. Anti-CP convalescent antibodies in sera from SA bacteremic patients in the placebo group during the phase III trial was evaluated as evidence for in vivo expression of CP during infection. Methods: Anti CP-5 and CP-8 IgG before and after infection was evaluated in ELISA. The affinity CP antibodies was evaluated in a thiocyanate binding assay and compared to the affinity of CP antibodies induced by StaphVAX(R). Results: Thirty seven isolates were received for typing. Of the 10 patients infected with type 5 SA, 4 had a >2 fold increase in CP-5 antibodies. None of these 10 showed any increase in antibodies to CP-8. Ten out of 20 patients with type 8 bacteremia had increased antibody titers to type 8 CP post-infection, while none of the 20 had any increase in antibodies to CP-5. Seven patients had type 336 bacteremia. None of these seven patients had any increase in convalescent antibodies to either CP-5 or 8. The concentration of thiocyanate required for 50% inhibition of antibody binding, was 0.4, 1.1, and 1.4M for type 5 pre-infection, post-infection, and post-%%%vaccination%%%, respectively. For type 8, the numbers were similar, 0.6, 1.6, and 1.4M, respectively. Conclusion: The increase in serotype specific antibodies after infection suggests that SA produces CP in vivo during infection. Moreover, convalescent antibodies and %%%vaccine%%%-induced antibodies have a higher affinity than the pre-existing antibodies.

7/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014381924 BIOSIS NO.: 200300338667
Pneumococcal bacteremia in a consortium of Veterans Affairs Medical Centers, VISN 15.
AUTHOR: Krueger T S (Reprint); Klotz S A; Bartholomew W; Powell B
AUTHOR ADDRESS: School of Pharmacy, University of Missouri - Kansas City, Kansas City, MO, USA**USA
JOURNAL: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy 42 p361 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy San Diego, CA, USA September 27-30, 2002; 20020927
SPONSOR: American Society for Microbiology
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: An ongoing, observational outcomes study of patients with bacteremia is being conducted in the Dept. of Veterans Affairs Veterans Integrated System Network (VISN) 15. Methods: Demographic, microbiology, pharmacy and outcomes data is being collected on all patients with bacterial and fungal isolates (single patient) from blood cultures, excluding patients with coagulase-negative %%%staphylococcal%%% isolates. Data was pooled from patients with Streptococcus pneumoniae

bacteremia in the 8 VISN hospitals from the years 1994 to 2001. Results: A total of 150 episodes of bacteremia were identified. The average age of the patient was 63 and overall mortality was 22%. There were 26 episodes of pneumococcal bacteremia in patients previously %%%vaccinated%%% (within 7 years) with the pneumococcal %%%polysaccharide%%% %%%vaccine%%% . The mortality was higher in this population than the unvaccinated group (30.7% vs. 20.1%), however, the average age of patients was higher in the %%%vaccinated%%% group (68 years vs. 62 years). Of those %%%vaccinated%%% patients that failed, 73% failed within 3 years of %%%vaccination%%%. Conclusion: Pneumococcal bacteremia is of concern in the %%%elderly%%% veteran population. In addition, it appears that patients who develop pneumococcal bacteremia despite %%%vaccination%%% with the %%%polysaccharide%%% %%%vaccine%%% may be at a higher risk of mortality.

7/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013706299 BIOSIS NO.: 200200299810
The safety and efficacy of a %%%staphylococcus%%% types 5 and 8 %%%polysaccharides%%% conjugate %%%vaccine%%% on %%%staphylococcus%%% bacteremia in %%%hemodialysis%%% patients
AUTHOR: Rasgon S A (Reprint); Yeoh H H (Reprint); Sheinfield H; Black S; Fatttom A I; Horwith G; Fuller S; Ordonez J; Law G; Johnson J; Alcorn H; Muenz L; Naso R
AUTHOR ADDRESS: Nephrology, Kaiser Permanente, Los Angeles, CA, USA**USA
JOURNAL: Journal of the American Society of Nephrology 12 (Program and Abstract Issue): p362A September, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: ASN (American Society of Nephrology)/ISN (International Society of Nephrology) World Congress of Nephrology San Francisco, CA, USA October 10-17, 2001; 20011010
SPONSOR: American Society of Nephrology
International Society of Nephrology
ISSN: 1046-6673
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Citation
LANGUAGE: English

7/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013607866 BIOSIS NO.: 200200201377
The role of the capsular %%%polysaccharide%%% adhesin (PS/A) virulence and immunoprophylaxis of S. aureus endocarditis in rats
AUTHOR: McKenney D (Reprint); Pouliot K L (Reprint); Maira-Latran T (Reprint); Kropec A (Reprint); Cramton S E; Goetz F; Goldmann D A; Pier G B (Reprint)
AUTHOR ADDRESS: Channing Laboratory, Boston, MA, USA**USA
JOURNAL: Abstracts of the General Meeting of the American Society for Microbiology 101 p284 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001; 20010520

SPONSOR: American Society for Microbiology
ISSN: 1060-2011
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have previously reported that the intercellular adhesion locus (ica) found in both S. epidermidis and S. aureus encodes proteins that synthesize PS/A and %%%polysaccharide%%% intercellular adhesin (PIA). These %%%polysaccharides%%% have the potential to be broadly protective %%%vaccines%%% against %%%staphylococcal%%% infections. Prior results showing protection against S. aureus in a mouse %%%renal%%% infection model were extended to investigate the role of PS/A in virulence in a rat model of endocarditis and the protective efficacy of PS/A in this model following active and passive immunization. Endocardial infection was induced by IV or IP injection of rats that had been catheterized via the carotid artery with a silastic catheter placed through the aortic valve. Rats were then infected IV with S. aureus 10833, S. aureus 10833Dica, a PS/A negative mutant and S. aureus 10833DELTAica (pSC38) which contains a plasmid containing the intact ica locus. After 7 days, rats that survived the infection period were assessed for infected valve vegetations. Infectious dose-50 (ID50) values were calculated for each strain. Rats infected with wild-type 10833 cells had an ID50 of less than 43 CFU compared to 6.9X106 CFU using the 10833DELTAica mutant. The ica-complemented strain had an ID50 of less than 120 CFU. 10 of 14 rats died when infected with wild-type 10833 compared to 0/16 rats infected with the 10833Dica strain (P=.00003). Protection studies showed that 1/9 rats actively immunized with PS/A were infected after challenge with the 10833 wild-type strain compared to 7/8 immunized with an irrelevant %%%polysaccharide%%% (P=.002). Rats passively immunized with antibodies to PS/A and challenged with wild-type strain10833 were protected against infection (3/7 positive) compared to animals given an irrelevant hyper-immune serum (7/7 positive, P=.03). Antibodies to PS/A did not protect against infection with strain10833DELTAica when a challenge dose sufficient to cause endocarditis was used. These results point to an important role of PS/A in virulence of S. aureus endocarditis and of the potential efficacy of antibodies to this material in preventing endocardial infection.

? ds

Set	Items	Description
S1	762	(TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
S2	295	RD S1 (unique items)
S3	680	STAPHYLOCOCC? AND VACCIN? AND POLYSACCHARIDE?
S4	452	RD S3 (unique items)
S5	833359	4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOSUPPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSPLANT OR SURICAL OR BURN)
S6	140	S4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOSUPPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSPLANT OR SURICAL OR BURN)
S7	140	RD S6 (unique items)

? t s7/7/6-140

7/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013581397 BIOSIS NO.: 200200174908
Use of a %%%Staphylococcus%%% aureus conjugate %%%vaccine%%% in patients receiving %%%hemodialysis%%%
AUTHOR: Shinefield Henry (Reprint); Black Steven; Fattom Ali; Horwith Gary; Rasgon Scott; Ordonez Juan; Yeoh Hock; Law David; Robbins John B; Schneerson Rachel; Muenz Larry; Naso Robert
AUTHOR ADDRESS: Kaiser Permanente Vaccine Study Center, 1 Kaiser Plaza, 16th Fl., Oakland, CA, 94612, USA**USA
JOURNAL: New England Journal of Medicine 346 (7): p491-496 February 14, 2002 2002
MEDIUM: print
ISSN: 0028-4793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: In patients with decreased resistance to infection, %%%Staphylococcus%%% aureus is a major cause of bacteremia and its complications. The capsular %%%polysaccharides%%% are essential for the pathogenesis of and immunity to S. aureus infection and are targets for %%%vaccines%%%. Methods: In a double-blind trial involving patients with end-stage %%%renal%%% disease who were receiving %%%hemodialysis%%%, we evaluated the safety, immunogenicity, and efficacy of a %%%vaccine%%% with S. aureus type 5 and 8 capsular %%%polysaccharides%%% conjugated to nontoxic recombinant Pseudomonas aeruginosa exotoxin A. Between April 1998 and August 1999, 1804 adult patients at 73 %%%hemodialysis%%% centers were randomly assigned to receive a single intramuscular injection of either %%%vaccine%%% or saline. IgG antibodies to S. aureus type 5 and 8 capsular %%%polysaccharides%%% were measured for up to two years, and episodes of S. aureus bacteremia were recorded. Efficacy was estimated by comparing the incidence of S. aureus bacteremia in the patients who received the %%%vaccine%%% with the incidence in the control patients. Results: Reactions to the %%%vaccine%%% were generally mild to moderate, and most resolved within two days. The capsular %%%polysaccharides%%% elicited an antibody response of at least 80 mug per milliliter (the estimated minimal level conferring protection) in 80 percent of patients for type 5 and in 75 percent of patients for type 8. The efficacy during weeks 3 to 54 was only 26 percent (P=0.23). However, between weeks 3 and 40 after %%%vaccination%%%, S. aureus bacteremia developed in 11 of 892 patients in the %%%vaccine%%% group who could be evaluated for bacteremia, as compared with 26 of 906 patients in the control group (estimate of efficacy, 57 percent; 95 percent confidence interval, 10 to 81 percent; nominal P=0.02). Conclusions: In patients receiving %%%hemodialysis%%%, a conjugate %%%vaccine%%% can confer partial immunity against S. aureus bacteremia for approximately 40 weeks, after which protection wanes as antibody levels decrease.

7/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013104812 BIOSIS NO.: 200100276651
Results from an efficacy study of Nabi(R) StaphVAX(R) (%%%Staphylococcus%%% aureus capsular %%%polysaccharide%%% (CP) conjugate %%%vaccine%%%) in %%%hemodialysis%%% patients

AUTHOR: Fattom Ali (Reprint); Horwith G; Fuller Steve; Black S; Shinefield H; Naso R
AUTHOR ADDRESS: Kaiser Permanante Vaccine Study Center, Oakland, CA, USA** USA
JOURNAL: Abstracts of Papers American Chemical Society 221 (1-2): pBIOT 45 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 221st National Meeting of the American Chemical Society San Diego, California, USA April 01-05, 2001; 20010401
SPONSOR: American Chemical Society
ISSN: 0065-7727
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

7/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012692688 BIOSIS NO.: 200000411001
Immune function and %%%vaccine%%% responses in healthy advanced %%%elderly%%% patients
AUTHOR: Carson Paul J; Nichol Kristin L; O'Brien James; Hilo Pierre; Janoff Edward N (Reprint)
AUTHOR ADDRESS: Infectious Disease Section, Veterans Affairs Medical Center, 1 Veterans Dr, Minneapolis, MN, 55417, USA**USA
JOURNAL: Archives of Internal Medicine 160 (13): p2017-2024 July 10, 2000 2000
MEDIUM: print
ISSN: 0003-9926
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: Decline in immune function has been reported to predictably accompany advancing age. However, to our knowledge, few studies have specifically characterized the rapidly expanding advanced %%%elderly%%% population or controlled adequately for concurrent diseases. Objective: To assess whether successfully reaching an advanced age in good health is associated with preserved immune function. Methods: We prospectively compared in vivo with in vitro variables of immune function in 29 healthy, independently living %%%elderly%%% subjects (mean age, 80 years; age range, 75-103 years) and in 21 healthy young control subjects (mean age, 29 years; age range, 25-35 years) in a Veterans Affairs Medical Center. Results: In vivo, among %%%elderly%%% and young subjects, numbers of total white blood cells, monocytes, lymphocytes, and lymphocyte subsets (CD4+ and CD8+ T lymphocytes and CD20+ B cells) were similar, as were levels of total serum IgG and IgM. Only levels of serum IgA were higher in the %%%elderly%%% subjects (3.0 vs 1.7 g/L; P = .001). Functionally, both groups showed vigorous responses to protein (tetanus and diphtheria toxoids) and %%%polysaccharide%%% (23-valent pneumococcal) %%%vaccines%%%. Although levels varied, the fold increases in %%%vaccine%%% antigen-specific IgG were not significantly different in young and %%%elderly%%% subjects, and the avidities of IgG to pneumococcal %%%polysaccharides%%% 14 and 19F were similar before and after %%%vaccination%%%. In vitro, proliferative responses of blood

0013706299 BIOSIS NO.: 200200299810
The safety and efficacy of a %%%staphylococcus%%% types 5 and 8 %%%polysaccharides%%% conjugate %%%vaccine%%% on %%%staphylococcus%%% bacteremia in %%%hemodialysis%%% patients
AUTHOR: Rasgon S A (Reprint); Yeoh H H (Reprint); Sheinfield H; Black S; Fatttom A I; Horwith G; Fuller S; Ordonez J; Law G; Johnson J; Alcorn H; Muenz L; Naso R
AUTHOR ADDRESS: Nephrology, Kaiser Permanente, Los Angeles, CA, USA**USA
JOURNAL: Journal of the American Society of Nephrology 12 (Program and Abstract Issue): p362A September, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: ASN (American Society of Nephrology)/ISN (International Society of Nephrology) World Congress of Nephrology San Francisco, CA, USA October 10-17, 2001; 20011010
SPONSOR: American Society of Nephrology
International Society of Nephrology
ISSN: 1046-6673
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Citation
LANGUAGE: English

0013581397 BIOSIS NO.: 200200174908
Use of a %%%Staphylococcus%%% aureus conjugate %%%vaccine%%% in patients receiving %%%hemodialysis%%%
AUTHOR: Shinefield Henry (Reprint); Black Steven; Fattom Ali; Horwith Gary; Rasgon Scott; Ordonez Juan; Yeoh Hock; Law David; Robbins John B; Schneerson Rachel; Muenz Larry; Naso Robert
AUTHOR ADDRESS: Kaiser Permanente Vaccine Study Center, 1 Kaiser Plaza, 16th Fl., Oakland, CA, 94612, USA**USA
JOURNAL: New England Journal of Medicine 346 (7): p491-496 February 14, 2002 2002
MEDIUM: print
ISSN: 0028-4793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

```
$%^Dialog;HighlightOn=%%%;HighlightOff=%%%;

Logging in to Dialog

Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ********
ENTER PASSWORD:
 ********
Welcome to DIALOG

Dialog level 04.01.00D

Last logoff:  20mar04 17:13:42
Logon file405 29mar04 09:06:42
           *** ANNOUNCEMENT ***
                    ***
--File 654 - US published applications from March 15, 2001 to the
present are now online.  Please see HELP NEWS 654 for details.

                    ***
--File 581 - The 2003 annual reload of Population Demographics is
complete. Please see Help News581 for details.

                   ***
--File 990 - NewsRoom now contains February 2003 to current records.
File 992 - NewsRoom 2003 archive has been newly created and contains
records from January 2003. The oldest months's records roll out of
File 990 and into File 992 on the first weekend of each month.
To search all 2003 records BEGIN 990, 992, or B NEWS2003, a new
OneSearch category.
                    ***
--Connect Time joins DialUnits as pricing options on Dialog.
See HELP CONNECT for information.
                    ***
                    ***
--SourceOne patents are now delivered to your email inbox
as PDF replacing TIFF delivery. See HELP SOURCE1 for more
information.
                    ***
--Important news for public and academic
libraries.  See HELP LIBRARY for more information.
                    ***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
                    ***
NEW FILES RELEASED
***DIOGENES: Adverse Drug Events Database (File 181)
***World News Connection (File 985)
***Dialog NewsRoom - 2003 Archive (File 992)
***TRADEMARKSCAN-Czech Republic (File 680)
***TRADEMARKSCAN-Hungary (File 681)
***TRADEMARKSCAN-Poland  (File 682)
                    ***
UPDATING RESUMED
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                    ***
RELOADED
***Medline (Files 154-155)
***Population Demographics -(File 581)
***CLAIMS Citation (Files 220-222)

REMOVED
                    ***

     >>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
     >>>    of new databases, price changes, etc.      <<<
                    ****
*
*
* ALL NEW CURRENT YEAR RANGES HAVE BEEN * * *
* * * INSTALLED   * * *
SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.9 term=ASCII
                      *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

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      /H = Help            /L = Logoff          /NOMENU = Command Mode


Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
? dialog
>>Invalid Option Number

                      *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

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      /H = Help             /L = Logoff          /NOMENU = Command Mode

Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
? b 410

       29mar04 09:06:44 User226352 Session D758.1
            $0.00    0.167 DialUnits FileHomeBase
     $0.00  Estimated cost FileHomeBase
     $0.00  Estimated cost this search
     $0.00  Estimated total session cost   0.167 DialUnits

File 410:Chronolog(R)  1981-2004/Apr
       (c) 2004 The Dialog Corporation

      Set  Items  Description
      ---  -----  -----------
? set hi %%%;set hi %%%
HILIGHT set on as '%%%'%%%
%%%HILIGHT set on as '%%%'
? b medicine
       29mar04 09:06:58 User226352 Session D758.2
            $0.00    0.074 DialUnits File410
     $0.00  Estimated cost File410
     $0.05  TELNET
     $0.05  Estimated cost this search
     $0.05  Estimated total session cost   0.242 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R)  1969-2004/Mar W3
         (c) 2004 BIOSIS
  File  34:SciSearch(R) Cited Ref Sci  1990-2004/Mar W3
         (c) 2004 Inst for Sci Info
  File  35:Dissertation Abs Online  1861-2004/Feb
         (c) 2004 ProQuest Info&Learning
  File  48:SPORTDiscus  1962-2004/Mar
         (c) 2004 Sport Information Resource Centre
  File  65:Inside Conferences  1993-2004/Mar W3
         (c) 2004 BLDSC all rts. reserv.
  File  71:ELSEVIER BIOBASE  1994-2004/Mar W2
         (c) 2004  Elsevier Science B.V.
  File  73:EMBASE  1974-2004/Mar W3
         (c) 2004 Elsevier Science B.V.
  File  91:MANTIS(TM)  1880-2003/Aug
         2001 (c) Action Potential
  File  94:JICST-EPlus  1985-2004/Mar W2
         (c)2004 Japan Science and Tech Corp(JST)
  File  98:General Sci Abs/Full-Text  1984-2004/Feb
         (c) 2004 The HW Wilson Co.
  File 135:NewsRx Weekly Reports  1995-2004/Mar W3
         (c) 2004 NewsRx
*File 135: New newsletters are now added. See Help News135 for the
complete list of newsletters.
  File 144:Pascal  1973-2004/Mar W3
         (c) 2004 INIST/CNRS
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  File 149:TGG Health&Wellness DB(SM)  1976-2004/Mar W3
        (c) 2004 The Gale Group
  File 155:MEDLINE(R)  1966-2004/Mar W3
        (c) format only 2004 The Dialog Corp.
*File 155: Medline has been reloaded. Accession numbers
have changed. Please see HELP NEWS 154 for details.
  File 156:ToxFile  1965-2004/Mar W4
        (c) format only 2004 The Dialog Corporation
  File 159:Cancerlit  1975-2002/Oct
        (c) format only 2002 Dialog Corporation
*File 159: Cancerlit ceases updating with immediate effect.
Please see HELP NEWS.
  File 162:Global Health  1983-2004/Feb
        (c) 2004 CAB International
  File 164:Allied & Complementary Medicine  1984-2004/Mar
        (c) 2004 BLHCIS
  File 172:EMBASE Alert  2004/Mar W3
        (c) 2004 Elsevier Science B.V.
  File 266:FEDRIP  2004/Feb
        Comp & dist by NTIS, Intl Copyright All Rights Res
  File 369:New Scientist  1994-2004/Mar W3
        (c) 2004 Reed Business Information Ltd.
  File 370:Science  1996-1999/Jul W3
        (c) 1999 AAAS
*File 370: This file is closed (no updates). Use File 47 for more current
information.
  File 399:CA SEARCH(R)  1967-2004/UD=14014
        (c) 2004 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
Alert feature enhanced for multiple files, etc. See HELP ALERT.
  File 434:SciSearch(R) Cited Ref Sci  1974-1989/Dec
        (c) 1998 Inst for Sci Info
  File 444:New England Journal of Med.  1985-2004/Mar W4
        (c) 2004 Mass. Med. Soc.
  File 467:ExtraMED(tm)  2000/Dec
        (c) 2001 Informania Ltd.
*File 467: For information about updating status please see Help News467.

      Set  Items  Description
      ---  -----  -----------
? s type(w)5 or type(w)8 and Staphylococc?
<------User Break------>
u!
? s (type(w)5 or type(w)8) and Staphylococc?
Processing
Processed  10 of  26 files ...
Processing
Processed  20 of  26 files ...
Processing
Completed processing all files
        5629469  TYPE
       12892540  5
          19534  TYPE(W)5
        5629469  TYPE
        6681934  8
           4257  TYPE(W)8
         426182  STAPHYLOCOCC?
```

```
      S1      762   (TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
? rd s1
...examined 50 records   (50)
...examined 50 records   (100)
...examined 50 records   (150)
...examined 50 records   (200)
...examined 50 records   (250)
...examined 50 records   (300)
...examined 50 records   (350)
...examined 50 records   (400)
...examined 50 records   (450)
...examined 50 records   (500)
...examined 50 records   (550)
...examined 50 records   (600)
...examined 50 records   (650)
>>>Record 266:210270 ignored; incomplete bibliographic data, not retained -
in RD set
...examined 50 records   (700)
...examined 50 records   (750)
...completed examining records
      S2      295   RD S1 (unique items)
? s staphylococc? and vaccin? and polysaccharide?
          426182   STAPHYLOCOCC?
          746152   VACCIN?
          311057   POLYSACCHARIDE?
      S3      680   STAPHYLOCOCC? AND VACCIN? AND POLYSACCHARIDE?
? rd s3
...examined 50 records   (50)
...examined 50 records   (100)
...examined 50 records   (150)
...examined 50 records   (200)
...examined 50 records   (250)
...examined 50 records   (300)
...examined 50 records   (350)
...examined 50 records   (400)
...examined 50 records   (450)
...examined 50 records   (500)
>>>Record 266:210270 ignored; incomplete bibliographic data, not retained -
in RD set
>>>Record 266:210268 ignored; incomplete bibliographic data, not retained -
in RD set
...examined 50 records   (550)
...examined 50 records   (600)
...examined 50 records   (650)
...completed examining records
      S4      452   RD S3 (unique items)
? ds

Set     Items   Description
S1        762   (TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
S2        295   RD S1 (unique items)
S3        680   STAPHYLOCOCC? AND VACCIN? AND POLYSACCHARIDE?
S4        452   RD S3 (unique items)
? s4 and (immunocomprom? or renal or hemodialysis or immunosuppress? or AIDS or
diabetic or neonates or elderly or transplant or surical or burn)
Processing
Processed  10 of  26 files ...
```

```
Processing
Processed  20 of  26 files ...
Completed processing all files
        12560743  4
           75588  IMMUNOCOMPROM?
         1633805  RENAL
          207169  HEMODIALYSIS
          514370  IMMUNOSUPPRESS?
          645032  AIDS
          527969  DIABETIC
          138662  NEONATES
          662383  ELDERLY
          367722  TRANSPLANT
              14  SURICAL
          119797  BURN
      S5  833359  4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR
                  IMMUNOSUPPRESS? OR AIDS OR DIABETIC OR NEONATES OR
                  ELDERLY OR TRANSPLANT OR SURICAL OR BURN)
? s s4 and (immunocomprom? or renal or hemodialysis or immunosuppress? or AIDS
or diabetic or neonates or elderly or transplant or surical or burn)
             452  S4
           75588  IMMUNOCOMPROM?
         1633805  RENAL
          207169  HEMODIALYSIS
          514370  IMMUNOSUPPRESS?
          645032  AIDS
          527969  DIABETIC
          138662  NEONATES
          662383  ELDERLY
          367722  TRANSPLANT
              14  SURICAL
          119797  BURN
      S6      140  S4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR
                  IMMUNOSUPPRESS? OR AIDS OR DIABETIC OR NEONATES OR
                  ELDERLY OR TRANSPLANT OR SURICAL OR BURN)
? rd s6
...examined 50 records  (50)
...examined 50 records  (100)
...completed examining records
      S7      140  RD S6 (unique items)
? ds

Set     Items   Description
S1        762   (TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
S2        295   RD S1 (unique items)
S3        680   STAPHYLOCOCC? AND VACCIN? AND POLYSACCHARIDE?
S4        452   RD S3 (unique items)
S5     833359   4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOSU-
             PPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSPL-
             ANT OR SURICAL OR BURN)
S6        140   S4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOS-
             UPPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSP-
             LANT OR SURICAL OR BURN)
S7        140   RD S6 (unique items)
? t s7/7/1-5

 7/7/1      (Item 1 from file: 5)
```

DIALOG(R)File 5:Biosis Previews(R)

0014778346 BIOSIS NO.: 200400145007
Development of StaphVAXTM, a %%%polysaccharide%%% conjugate %%%vaccine%%% against S. aureus infection: From the lab bench to phase III clinical trials.
AUTHOR: Fattom Ali I (Reprint); Horwith Gary; Fuller Steve; Propst Myra; Naso Robert
AUTHOR ADDRESS: NABI Biopharmaceuticals, 12280 Wilkins Avenue, Rockville, MD, 20852, USA**USA
AUTHOR E-MAIL ADDRESS: afattom@nabi.com
JOURNAL: Vaccine 22 (7): p880-887 17 February, 2004 2004
MEDIUM: print
ISSN: 0264-410X (ISSN print)
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Staphylococcus%%% aureus is the most common nosocomial pathogen and is responsible for approximately one-third of hospital-acquired bacteremias. The emergence of strains with multidrug resistance, including resistance to vancomycin, the antibiotic of last resort, presents the medical community with a major public health problem. Alternative therapies, including immunotherapy, have been in development for several decades. The discovery of S. aureus capsular %%%polysaccharides%%% from clinical isolates, and their importance to pathogenicity via antiphagocytic activity, opened a new window of opportunity for development of %%%vaccines%%% and immunotherapy against this pathogen. A conjugate %%%vaccine%%%, StaphVAXTM that includes the two most prevalent capsular %%%polysaccharides%%%, types 5 and 8, coupled to a carrier protein efficient in promoting a Th2 response, was developed. In a recent phase III clinical study in %%%hemodialysis%%% patients, StaphVAXTM was shown to prevent S. aureus bacteremia for up to 10 months following a single immunization. The history, epidemiology, serology, and development of StaphVAXTM, including preclinical and clinical studies demonstrating efficacy are described in this review.

7/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014388995 BIOSIS NO.: 200300347714
In vivo production of capsular %%%polysaccharide%%% (CP) production as evidenced by type specific antibody increase following %%%Staphylococcus%%% aureus (SA) bacteremia in %%%hemodialysis%%% patients.
AUTHOR: Fattom A I (Reprint); Wu Y (Reprint); Propst M (Reprint); Fuller S (Reprint); Horwith G (Reprint); Naso R (Reprint)
AUTHOR ADDRESS: Nabi Biopharmaceuticals, Rockville, MD, USA**USA
JOURNAL: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy 42 p238 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy San Diego, CA, USA September 27-30, 2002; 20020927
SPONSOR: American Society for Microbiology

DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: StaphVAX(R), a conjugate %%%vaccine%%% containing types 5 and 8 SA CP, demonstrated significant protection against SA bacteremia in %%%hemodialysis%%% patients. Anti-CP convalescent antibodies in sera from SA bacteremic patients in the placebo group during the phase III trial was evaluated as evidence for in vivo expression of CP during infection. Methods: Anti CP-5 and CP-8 IgG before and after infection was evaluated in ELISA. The affinity CP antibodies was evaluated in a thiocyanate binding assay and compared to the affinity of CP antibodies induced by StaphVAX(R). Results: Thirty seven isolates were received for typing. Of the 10 patients infected with type 5 SA, 4 had a >2 fold increase in CP-5 antibodies. None of these 10 showed any increase in antibodies to CP-8. Ten out of 20 patients with type 8 bacteremia had increased antibody titers to type 8 CP post-infection, while none of the 20 had any increase in antibodies to CP-5. Seven patients had type 336 bacteremia. None of these seven patients had any increase in convalescent antibodies to either CP-5 or 8. The concentration of thiocyanate required for 50% inhibition of antibody binding, was 0.4, 1.1, and 1.4M for type 5 pre-infection, post-infection, and post-%%%vaccination%%%, respectively. For type 8, the numbers were similar, 0.6, 1.6, and 1.4M, respectively. Conclusion: The increase in serotype specific antibodies after infection suggests that SA produces CP in vivo during infection. Moreover, convalescent antibodies and %%%vaccine%%%-induced antibodies have a higher affinity than the pre-existing antibodies.

7/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014381924 BIOSIS NO.: 200300338667
Pneumococcal bacteremia in a consortium of Veterans Affairs Medical Centers, VISN 15.
AUTHOR: Krueger T S (Reprint); Klotz S A; Bartholomew W; Powell B
AUTHOR ADDRESS: School of Pharmacy, University of Missouri - Kansas City, Kansas City, MO, USA**USA
JOURNAL: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy 42 p361 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy San Diego, CA, USA September 27-30, 2002; 20020927
SPONSOR: American Society for Microbiology
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: An ongoing, observational outcomes study of patients with bacteremia is being conducted in the Dept. of Veterans Affairs Veterans Integrated System Network (VISN) 15. Methods: Demographic, microbiology, pharmacy and outcomes data is being collected on all patients with bacterial and fungal isolates (single patient) from blood cultures, excluding patients with coagulase-negative %%%staphylococcal%%% isolates. Data was pooled from patients with Streptococcus pneumoniae

bacteremia in the 8 VISN hospitals from the years 1994 to 2001. Results: A total of 150 episodes of bacteremia were identified. The average age of the patient was 63 and overall mortality was 22%. There were 26 episodes of pneumococcal bacteremia in patients previously %%%vaccinated%%% (within 7 years) with the pneumococcal %%%polysaccharide%%% %%%vaccine%%% . The mortality was higher in this population than the unvaccinated group (30.7% vs. 20.1%), however, the average age of patients was higher in the %%%vaccinated%%% group (68 years vs. 62 years). Of those %%%vaccinated%%% patients that failed, 73% failed within 3 years of %%%vaccination%%%. Conclusion: Pneumococcal bacteremia is of concern in the %%%elderly%%% veteran population. In addition, it appears that patients who develop pneumococcal bacteremia despite %%%vaccination%%% with the %%%polysaccharide%%% %%%vaccine%%% may be at a higher risk of mortality.

7/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013706299 BIOSIS NO.: 200200299810
The safety and efficacy of a %%%staphylococcus%%% types 5 and 8 %%%polysaccharides%%% conjugate %%%vaccine%%% on %%%staphylococcus%%% bacteremia in %%%hemodialysis%%% patients
AUTHOR: Rasgon S A (Reprint); Yeoh H H (Reprint); Sheinfield H; Black S; Fatttom A I; Horwith G; Fuller S; Ordonez J; Law G; Johnson J; Alcorn H; Muenz L; Naso R
AUTHOR ADDRESS: Nephrology, Kaiser Permanente, Los Angeles, CA, USA**USA
JOURNAL: Journal of the American Society of Nephrology 12 (Program and Abstract Issue): p362A September, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: ASN (American Society of Nephrology)/ISN (International Society of Nephrology) World Congress of Nephrology San Francisco, CA, USA October 10-17, 2001; 20011010
SPONSOR: American Society of Nephrology
International Society of Nephrology
ISSN: 1046-6673
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Citation
LANGUAGE: English

7/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013607866 BIOSIS NO.: 200200201377
The role of the capsular %%%polysaccharide%%% adhesin (PS/A) virulence and immunoprophylaxis of S. aureus endocarditis in rats
AUTHOR: McKenney D (Reprint); Pouliot K L (Reprint); Maira-Latran T (Reprint); Kropec A (Reprint); Cramton S E; Goetz F; Goldmann D A; Pier G B (Reprint)
AUTHOR ADDRESS: Channing Laboratory, Boston, MA, USA**USA
JOURNAL: Abstracts of the General Meeting of the American Society for Microbiology 101 p284 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001; 20010520

SPONSOR: American Society for Microbiology
ISSN: 1060-2011
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have previously reported that the intercellular adhesion locus (ica) found in both S. epidermidis and S. aureus encodes proteins that synthesize PS/A and %%%polysaccharide%%% intercellular adhesin (PIA). These %%%polysaccharides%%% have the potential to be broadly protective %%%vaccines%%% against %%%staphylococcal%%% infections. Prior results showing protection against S. aureus in a mouse %%%renal%%% infection model were extended to investigate the role of PS/A in virulence in a rat model of endocarditis and the protective efficacy of PS/A in this model following active and passive immunization. Endocardial infection was induced by IV or IP injection of rats that had been catheterized via the carotid artery with a silastic catheter placed through the aortic valve. Rats were then infected IV with S. aureus 10833, S. aureus 10833Dica, a PS/A negative mutant and S. aureus 10833DELTAica (pSC38) which contains a plasmid containing the intact ica locus. After 7 days, rats that survived the infection period were assessed for infected valve vegetations. Infectious dose-50 (ID50) values were calculated for each strain. Rats infected with wild-type 10833 cells had an ID50 of less than 43 CFU compared to 6.9X106 CFU using the 10833DELTAica mutant. The ica-complemented strain had an ID50 of less than 120 CFU. 10 of 14 rats died when infected with wild-type 10833 compared to 0/16 rats infected with the 10833Dica strain (P=.00003). Protection studies showed that 1/9 rats actively immunized with PS/A were infected after challenge with the 10833 wild-type strain compared to 7/8 immunized with an irrelevant %%%polysaccharide%%% (P=.002). Rats passively immunized with antibodies to PS/A and challenged with wild-type strain10833 were protected against infection (3/7 positive) compared to animals given an irrelevant hyper-immune serum (7/7 positive, P=.03). Antibodies to PS/A did not protect against infection with strain10833DELTAica when a challenge dose sufficient to cause endocarditis was used. These results point to an important role of PS/A in virulence of S. aureus endocarditis and of the potential efficacy of antibodies to this material in preventing endocardial infection.

? ds

Set	Items	Description
S1	762	(TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
S2	295	RD S1 (unique items)
S3	680	STAPHYLOCOCC? AND VACCIN? AND POLYSACCHARIDE?
S4	452	RD S3 (unique items)
S5	833359	4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOSUPPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSPLANT OR SURICAL OR BURN)
S6	140	S4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOSUPPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSPLANT OR SURICAL OR BURN)
S7	140	RD S6 (unique items)

? t s7/7/6-140

7/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0010946962 BIOSIS NO.: 199799581022
Response of end stage %%%renal%%% disease patients to increasing doses of S. aureus %%%vaccine%%%
AUTHOR: Johnson J (Reprint); Fries L; Abboud H; Heyka R
AUTHOR ADDRESS: NABI, Rockville, MD, USA**USA
JOURNAL: Abstracts of the General Meeting of the American Society for Microbiology 97 (0): p43 1997 1997
CONFERENCE/MEETING: 97th General Meeting of the American Society for Microbiology Miami Beach, Florida, USA May 4-8, 1997; 19970504
ISSN: 1060-2011
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Citation
LANGUAGE: English

0010276254 BIOSIS NO.: 199698744087
Safety and immunogenicity of %%%Staphylococcus%%% aureus type 5 capsular %%%polysaccharide%%%-Pseudomonas aeruginosa recombinant exoprotein A conjugate %%%vaccine%%% in patients on %%%hemodialysis%%%
AUTHOR: Welch Paul G; Fattom Ali; Moore Jack Jr; Schneerson Rachel; Shiloach Joseph; Bryla Dolores A; Li Xiuru; Robbins John B (Reprint)
AUTHOR ADDRESS: National Inst. Health, Public Halth Service, Building 6, Room 424, National Inst. Child Health Human Dev., Bethesda, MD 20892, USA **USA
JOURNAL: Journal of the American Society of Nephrology 7 (2): p247-253 1996 1996
ISSN: 1046-6673
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

0010260246 BIOSIS NO.: 199698728079
%%%Staphylococcal%%% %%%vaccines%%%: A realistic dream
AUTHOR: Fattom Ali I (Reprint); Naso Robert
AUTHOR ADDRESS: W. W. Karakawa Microbial Pathogenesis Lab., Univax Biologics Inc., 12280 Wilkins Ave., Rockville, MD 20852, USA**USA
JOURNAL: Annals of Medicine 28 (1): p43-46 1996 1996
ISSN: 0785-3890
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Staphylococcus%%% aureus, especially multidrug resistant strains, continues to be a leading cause of serious nosocomial infections. In spite of the debate among investigators in the field, the discovery of serologically distinct capsular %%%polysaccharides%%% on the surface of clinical isolates has renewed the prospects for development of %%%vaccines%%% and passive protective immunity against S. aureus infections. Capsular %%%polysaccharide%%% conjugate %%%vaccines%%% have now been produced and proven to be safe and immunogenic in both healthy and in a significant percentage of %%%immunocompromised%%% patients. Antibodies generated in humans against these %%%vaccines%%% have been shown to mediate type-specific opsonophagocytosis, and to protect animals against lethal challenge with the appropriate S. aureus isolate.

0010130787 BIOSIS NO.: 199698598620
Effect of conjugation methodology, carrier protein, and adjuvants on the immune response to %%%Staphylococcus%%% aureus capsular %%%polysaccharides%%%
AUTHOR: Fattom Ali (Reprint); Li Xiuru; Cho Yu Hee; Burns Amy; Hawwari Abbas; Shepherd Sara E; Coughlin Richard; Winston Scott; Naso Robert
AUTHOR ADDRESS: W. W. Karakawa Microbial Pathogenesis Lab., Univax Biol. Inc., Rockville, MD, USA**USA
JOURNAL: Vaccine 13 (14): p1288-1293 1995 1995
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Conjugate %%%vaccines%%% were prepared with S. aureus type 8 capsular %%%polysaccharide%%% (CP) using three carrier proteins: Pseudomonas aeruginosa exotoxin A (ETA), a non-toxic recombinant ETA (rEPA), and diphtheria toxoid (DTd). Adipic acid dihydrazide (ADH) or N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) was used as a spacer to link the CP to carrier protein. All conjugates gave a high immune response with a boost after the second immunization. Conjugates prepared with ADH gave higher antibody titers than conjugates prepared with SPDP. IgG, was the primary subclass elicited by all conjugates regardless of the carrier protein or the conjugation method used to prepare the %%%vaccines%%%. The non-immunogenic CP and the conjugates were formulated with either monophosphoryl lipid A (MPL), QS21, or in Novasomes and evaluated in mice. While the adjuvants failed to improve the immunogenicity of the nonconjugated CP, a more than fivefold increase in the antibody levels was observed when these adjuvants were used with the conjugates. Significant rises in IgG-2b and IgG-3 were observed with all formulations. The enhancement of the immunogenicity and the IgG subclass shift, as seen with some adjuvants, mail, prove to be important in %%%immunocompromised%%% patients.

0010021564 BIOSIS NO.: 199598489397
Prevention of systemic infections caused by group B streptococcus and %%%Staphylococcus%%% aureus by multivalent %%%polysaccharide%%%-protein conjugate %%%vaccines%%%
BOOK TITLE: Annals of the New York Academy of Sciences; Combined %%%vaccines%%% and simultaneous administration: Current issues and perspectives
AUTHOR: Robbins John B (Reprint); Schneerson Rachel (Reprint); Vann Willie F; Bryla Dolores A (Reprint); Fattom Ali
BOOK AUTHOR/EDITOR: Williams J C (Editor); Goldenthal K L (Editor); Burns D L (Editor); Lewis B P Jr (Editor)
AUTHOR ADDRESS: Natl. Inst. Child Health Hum. Dev., Natl. Inst. Health, Bethesda, MD 20892, USA**USA
SERIES TITLE: Annals of the New York Academy of Sciences 754 p68-82 1995
BOOK PUBLISHER: New York Academy of Sciences (a), 2 East 63rd Street, New York, New York 10021, USA
CONFERENCE/MEETING: Conference Bethesda, Maryland, USA July 28-30, 1993; 19930728
ISSN: 0077-8923 ISBN: 0-89766-863-4
DOCUMENT TYPE: Book; Meeting; Book Chapter; Meeting Paper
RECORD TYPE: Citation
LANGUAGE: English

0008679952 BIOSIS NO.: 199345110940
Safety and immunogenicity of a conjugate %%%vaccine%%% against %%%Staphylococcus%%% aureus type 5 capsular %%%polysaccharide%%% in %%%hemodialysis%%% (HD) patients
AUTHOR: Welch P; Fattom A; Sigmon J; Schneerson R; Robbins J; Moore J
AUTHOR ADDRESS: Nephrol. and DCI, Walter Reed AMC, Washington, DC, USA**USA
JOURNAL: Journal of the American Society of Nephrology 4 (3): p259 1993
CONFERENCE/MEETING: 26th Annual Meeting of the ASN (American Society of Nephrology) Boston, Massachusetts, USA November 14-17, 1993; 19931114
ISSN: 1046-6673
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: English

01465379 Genuine Article#: HA564 Number of References: 38
Title: COMPARATIVE IMMUNOGENICITY OF CONJUGATES COMPOSED OF THE %%%STAPHYLOCOCCUS%%%-AUREUS TYPE-8 CAPSULAR %%%POLYSACCHARIDE%%% BOUND TO CARRIER PROTEINS BY ADIPIC ACID DIHYDRAZIDE OR N-SUCCINIMIDYL-3-(2-PYRIDYLDITHIO)PROPIONATE
Author(s): FATTOM A; SHILOACH J; BRYLA D; FITZGERALD D; PASTAN I; KARAKAWA WW; ROBBINS JB; SCHNEERSON R
Corporate Source: NICHHD,DEV & MOLEC IMMUN LAB/BETHESDA//MD/20892; NICHHD,DEV & MOLEC IMMUN LAB/BETHESDA//MD/20892; NICHHD,BIOMETRY & MATH STAT BRANCH/BETHESDA//MD/20892; NIDDKD,BIOTECHNOL UNIT/BETHESDA//MD/20892; NCI,MOLEC BIOL LAB/BETHESDA//MD/20892; PENN STATE UNIV,DEPT BIOCHEM/UNIV PK//PA/16802
Journal: INFECTION AND IMMUNITY, 1992, V60, N2 (FEB), P584-589
Language: ENGLISH Document Type: ARTICLE

Infections diseases

MALADIES INFECTIEUSES
Erard Ph.
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Medecine et Hygiene (MED. HYG.) (Switzerland) 14 JAN 2004, 62/2465 (106-110)
CODEN: MEHGA ISSN: 0025-6749
DOCUMENT TYPE: Journal ; Review
LANGUAGE: FRENCH SUMMARY LANGUAGE: ENGLISH; FRENCH
NUMBER OF REFERENCES: 35

Several important therapeutic advances and insights into the natural history of infectious diseases have been produced in the year 2003. The role of corticosteroids for the treatment of bacterial meningitis in adults, if given prior to or concurrently with antibiotics, has been established. The use of antibiotics in upper respiratory tract infections remains problematic, too frequent and too large-spectrum. Antivirals are efficacious for influenza infection if given early (ideally within 12 hours after onset of symptoms). Pneumococcal %%%vaccine%%% protects against bacteremic pneumococcal infections, not against non-bacteremic pneumonia. As shown by a recent controlled trial, treatment of asymptomatic bacteriuria in %%%diabetic%%% patients shows no benefit. The mortality associated with MRSA bacteremias is higher than with methicillin-susceptible S. aureus isolates.

11540353 EMBASE No: 2002112001

Conjugated %%%vaccine%%% provides partial immunity to %%%Staphylococcus%%% aureus

Pharmaceutical Journal (PHARM. J.) (United Kingdom) 02 MAR 2002, 268/7187 (279)
CODEN: PHJOA ISSN: 0031-6873
DOCUMENT TYPE: Journal ; Note
LANGUAGE: ENGLISH

06661387 EMBASE No: 1996326264

%%%Staphylococcus%%% aureus %%%vaccination%%% for dialysis patients - An update

Fattom A.I.; Naso R.
12280 Wilkins Ave,Rockville, MD 20852 United States

Advances in Renal Replacement Therapy (ADV. RENAL REPLACEMENT THER.) (United States) 1996, 3/4 (302-308)
CODEN: ARRTF ISSN: 1073-4449
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

%%%Staphylococcus%%% aureus infections are a major cause of morbidity in both %%%hemodialysis%%% and peritoneal dialysis patients. The availability of a safe and effective protective %%%vaccine%%% would be of great benefit to these patients, but attempts at using %%%vaccines%%% consisting of inactivated whole cells have been unsuccessful. This article discusses an alternate approach to S. aureus %%%vaccine%%% design using a capsular %%%polysaccharide%%% conjugate and preliminary results in %%%hemodialysis%%% and peritoneal patients.

0000049807 (THIS IS THE FULLTEXT)
Prevention of Nasal Colonization Could Eliminate Disease in High Risk Patients
TB & Outbreaks Week, August 15-22, 2000, p.11

DOCUMENT TYPE: Research News LANGUAGE: English
RECORD TYPE: FULLTEXT
AUDIENCE: Consumer
WORD COUNT: 416

TEXT: The anterior portion of the nasal passages is a prime site for colonization by %%%Staphylococcus%%% aureus Scientists at Harvard Medical School's Brigham and Women's Hospital maintain that by eliminating colonization in this area, the chance for infection in high risk individuals can be reduced.

Those at risk for S. aureus infections include surgery and dialysis patients, individuals with diabetes, and people infected with the human immunodeficiency virus (HIV).

Kevin Kiser and co-authors of this study that looked at potential immunization strategies against S. aureus nasal colonization in mice, reported their findings at the 100 th General Meeting of the American Society for Microbiology, held in Los Angeles, California.

"Because of the emergence of strains of S. aureus resistant to multiple antibiotics including mupirocin-resistant and vancomycin-tolerant MRSA, nosocomial epidemics are of great concern," researchers said.

Initially, the investigators used a killed bacteria %%%vaccine%%% that they introduced via the nasal passages to induce the creation of antibodies in the serum and saliva of the mice. Control mice were inoculated with a plain phosphate buffered saline (PBS) solution. These mice were then challenged intranasally with a strain of bacteria known as S. aureus Reynolds.

0000041492 (THIS IS THE FULLTEXT)
Clinical Trial Data for
Biotech Week, October 4-11, 2000, p.24-25

DOCUMENT TYPE: Research News LANGUAGE: English
RECORD TYPE: FULLTEXT
AUDIENCE: Professional
WORD COUNT: 445

TEXT: Nabi announced preliminary results from the Phase III clinical trial for StaphVAXTM (%%%Staphylococcus%%% aureus conjugate %%%vaccine%%%) at the 40th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Toronto, Canada.

The data from the trial demonstrated a dramatic reduction in S. aureus bacteremias (blood stream infections) during the first 10 months of the study. However, the decrease in bloodstream infections after one-year follow up, the primary endpoint for the study, did not achieve statistical significance.

The study was performed by the Kaiser Permanente %%%Vaccine%%% Study Center based in Oakland, California, and the preliminary results were presented by the principal investigators from that institution, Steven Black, MD, and Henry Shinefield, MD.

In reviewing the preliminary results from the trial, Black stated, "Through 10 months, the study results found 57% fewer cases of S. aureus disease in these immune compromised study participants who received the %%%vaccine%%%. S. aureus is an increasing, lethal bacterium, which causes significant morbidity and mortality."

Shinefield affirmed, "These results are particularly important at a time of growing resistance of S. aureus to antibiotics."

StaphVAX consists of capsular %%%polysaccharides%%% (CPS) from the two most common serotypes of S. aureus (Type 5 and Type 8), each conjugated to a carrier protein. The double-blinded, placebo-controlled trial involved 1,804 end-stage %%%renal%%% disease patients on %%%hemodialysis%%% who were randomly assigned so that approximately half were %%%vaccinated%%% with a single intramuscular injection of StaphVAX and half received a placebo %%%vaccination%%%.

Investigators observed %%%vaccinated%%% patients for at least one year to collect information on bloodstream infections that might occur. In the group of patients that received placebo there were 17 S. aureus bacteremias at approximately six months of follow-up, compared to seven bacteremias in the group that received StaphVAX or a 58% reduction in S. aureus bacteremias ($p = 0.0438$).

0000029699 (THIS IS THE FULLTEXT)
Enterococcal %%%Vaccine%%% Featured at American Society for Microbiology
Vaccine Weekly, May 11, 1998, p.17-18

DOCUMENT TYPE: Editor's Choice LANGUAGE: English
RECORD TYPE: FULLTEXT
AUDIENCE: Professional
WORD COUNT: 485

TEXT: Nabi, Boca Raton, Florida, announced that an abstract written by Nabi scientists describing its enterococcal %%%vaccine%%% and the protective effect of antibodies raised by the %%%vaccine%%% is to be featured at the Annual Meeting of the American Society for Microbiology (ASM), scheduled to be held in Atlanta, Georgia, in May 1998.

The abstract, entitled "Antibodies to an Enterococcus Type 1 Capsular %%%Polysaccharide%%% Clear Bacteremia and Organ Seeding in Mice Challenged with a Sublethal Dose of E. faecalis Bacteria" is among those selected by the ASM Public Communications Committee and General Meeting Program Committee to be highlighted in the press room at the ASM Annual Meeting. The study shows the ability of polyclonal antibodies raised using the enterococcal %%%vaccine%%% to protect mice from challenge with a vancomycin-resistant clinical isolate of Enterococcus faecalis.

Enterococcal species are a major cause of urinary tract infections, wound infections, intra-abdominal abscesses, endocarditis, bacteremia and a variety of nosocomial infections including bacterial sepsis in newborns. The enterococci are members of the normal gastrointestinal tract flora of humans.

Hospital-acquired enterococcal infections are associated with increasing morbidity and mortality due to their resistance to frequently-used broad-spectrum antibiotics. The increasing incidence of resistance of these bacteria to vancomycin, long considered as the last effective bacteriostatic agent with which to combat enterococcal infections, has led to the need for development of alternative drugs to prevent and treat such infections.

A surface %%%polysaccharide%%%, called ENT-1, has been identified by Nabi researchers on the surface of an estimated 80 percent of Enterococcus faecalis clinical isolates. E. faecalis is the cause of approximately 80 percent of all enterococcal infections in hospital settings. ENT-1 has been made immunogenic by cross-linking it to a carrier protein, and the resultant %%%vaccine%%% was used in rabbits to raise antibodies with high reactivity to E. faecalis ENT-1. Injection of the antibody into mice protected them from bacteremia and organ abscesses caused by E. faecalis upon challenge with a vancomycin-resistant clinical isolate of the bacteria.

"Protection of animals by passive immunization as described in this study is considered crucial for the continued development of this %%%vaccine%%%," commented Dr. Robert Naso, Nabi. "The company expects to develop this drug both as a stand-alone %%%vaccine%%% and to generate an antibody-based product to treat patients who cannot respond to a %%%vaccine%%%, either because they are %%%immunocompromised%%% or because they are at immediate risk of infection and don't have time to respond to a %%%vaccine%%%."

David Gury, Nabi, stated, "We are excited about the discovery and effects of this enterococcal %%%vaccine%%% and are committed to its further development. We believe that this %%%vaccine%%% and antibodies generated in plasma donors by this %%%vaccine%%% will provide products that will complement our Nabi-StaphVAX and Nabi-Altastaph products which are

currently in clinical studies for the prevention of %%%staphylococcal%%% infections in hospitalized and other at-risk patients."

7/7/50 (Item 14 from file: 135)
DIALOG(R)File 135:NewsRx Weekly Reports

0000029550 (THIS IS THE FULLTEXT)
%%%Vaccine%%% Targets Vancomycin-Resistant Bacteria
DeNoon, Daniel J.
AIDS Weekly, May 11, 1998, p.5-6

DOCUMENT TYPE: Editor's Choice LANGUAGE: English
RECORD TYPE: FULLTEXT
AUDIENCE: Professional
WORD COUNT: 441

TEXT: Antibodies to a new %%%vaccine%%% antigen protected mice against challenge with a clinical isolate of a vancomycin-resistant bacterium.

Vancomycin is the last line of defense against organisms that have acquired resistance to antimicrobial drugs. Species of Enterococcus faecalis - which occur among the normal intestinal flora of humans - are a major cause of urinary tract infections, wound infections, intra-abdominal abscesses, endocarditis, bacteremia, and many hospital-acquired infections including bacterial sepsis of newborns. An increasing number of these infections are caused by enterococci that have developed resistance to vancomycin.

Early animal studies show that antibodies to a candidate %%%vaccine%%% antigen of enterococcus type 1 - present on some 80 percent of enterococcal species, including those with vancomycin resistance - can protect mice against non-lethal enterococcal challenge.

"Protection of animals by passive immunization as described in this study is considered crucial for the continued development of this %%%vaccine%%%," said Robert Naso, co-author of the study and vice president of the biotechnology firm Nabi, Boca Raton, Florida.

"The company expects to develop this drug both as a stand-alone %%%vaccine%%% and to generate an antibody-based product to treat patients who cannot respond to a %%%vaccine%%%, either because they are %%%immunocompromised%%% or because they are at immediate risk of infection and don't have time to respond to a %%%vaccine%%%."

The studies, announced by Nabi, are scheduled for presentation at the upcoming 98th General Meeting of the American Society for Microbiology, to be held May 17-21, 1998, in Atlanta, Georgia.

Nabi researchers R.K. Sood and colleagues showed that a capsular %%%polysaccharide%%% (CP), ENT-1, appeared on 60 of 67 geographically diverse isolates of E. faecalis , including vancomycin-resistant strains. When conjugated to diphtheria toxoid, the antigen was immunogenic in rabbits and in mice.

"The presence of this CP on the surface of the majority of vancomycin-sensitive and vancomycin-resistant isolates and the ability of CP-specific antibodies to mediate opsonic killing of these isolates by human phagocytes make this CP an excellent %%%vaccine%%% candidate against E. faecalis infections," Sood et al. wrote in their presentation abstract.

Nabi researcher A. Ortiz and colleagues subsequently showed that passive immunization of mice with antibodies to ENT-1 conferred protection

against E. faecalis bacterial challenge.

Nabi currently manufactures three approved immunotherapeutic products: Autoplex-T, an anti-inhibitor coagulant complex for the treatment of hemophilia; H-BIG, hepatitis B immune globulin for passive immunization against hepatitis B; and WinRho SDF, Rh (D) intravenous immune globulin for the treatment of immune thrombocytopenic purpura (ITP). It is currently developing %%%vaccine%%% products for active and passive %%%vaccination%%% against %%%staphylococcal%%% infections. - by Daniel J. DeNoon, Senior Editor

7/7/51 (Item 15 from file: 135)
DIALOG(R)File 135:NewsRx Weekly Reports

0000009059 (THIS IS THE FULLTEXT)
StaphVAX May Protect Against Fatal Staph Infections
Vaccine Weekly, September 30, 1996, p.10

DOCUMENT TYPE: Editor's Choice LANGUAGE: English
RECORD TYPE: FULLTEXT
AUDIENCE: Professional
WORD COUNT: 409

TEXT: NABI, Boca Raton, Florida, announced positive results of its ongoing Phase II Dosing Study of StaphVAX (S. aureus Type 5 and 8 Capsular %%%Polysaccharide%%% Conjugate %%%Vaccine%%%).

StaphVAX is a proprietary %%%vaccine%%% for the prevention of %%%Staphylococcus%%% aureus (staph) infection. Analysis of the interim data showed that StaphVAX was well tolerated in all trial participants and StaphVAX demonstrated the ability to stimulate significant levels of staph fighting antibodies in End Stage %%%Renal%%% Disease (ESRD) patients.

David J. Gury, NABI, announced at the Donaldson Lufkin & Jenrette Conference in New York, New York, that "This study is an important milestone in the ongoing battle against staph infections. The ability of StaphVAX to stimulate the production of high levels of staph fighting antibodies in ESRD patients suggests that our product may have the ability to prevent thousands of high risk patients from developing potentially fatal staph infections."

Gury added, "StaphVAX targets two predominant types of staph aureus, which together comprise at least 80 percent of all staph aureus infections. Moving forward, we will utilize the data gathered in this study to select the optimum dosing levels for the most expeditious clinical development of this product through pivotal clinical trials." Gury noted that the company has scheduled to present a full analysis of these data at the American Society of Microbiology, General Meeting, to be held in Miami, Florida, in May 1997.

These results are consistent with NABI's objective to prove that StaphVAX can stimulate antibody levels in ESRD patients comparable to the levels of antibodies stimulated in healthy donors. In addition, analysis of the data indicates that StaphVAX is able to sustain heightened antibody levels in ESRD patients for at least three months.

Staph bacteria are present on the skin and are harmless until the skin is broken during trauma, surgery or IV catheterization. When staph bacteria gain access to deeper tissue, they can cause serious infections, such as bacteremia, endocarditis, meningitis, osteomyelitis, pneumonia, and

peritonitis.

Staph is rampant in hospitals, afflicting millions of people per year in the United States, including patients experiencing severe trauma, or undergoing kidney dialysis, cardiac surgery or prosthetic surgery. Strains of staph are becoming resistant to current antibiotics.

NABI management noted that this multicenter randomized Phase II Dosing Study was designed to evaluate two separate high doses of StaphVAX in 33 adult patients undergoing %%%hemodialysis%%% and suffering from ESRD. The tolerability of StaphVAX when administered as an intramuscular injection was also evaluated and confirmed.

7/7/52 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

12442231 PASCAL No.: 96-0099021

Effect of conjugation methodology, carrier protein, and adjuvants on the immune response to Staphyloccus aureus capsular %%%polysaccharides%%%

ALI FATTOM; XIURU LI; YUN HEE CHO; BURNS A; HAWWARI A; SHEPHERD S E; COUGHLIN R; WINSTON S; NASO R

Univax Biologics Inc., Karakawa microbial pathogenesis lab., Rockville MD , USA

Journal: Vaccine, 1995, 13 (14) 1288-1293

ISSN: 0264-410X CODEN: VACCDE Availability: INIST-20289; 354000055561550030

No. of Refs.: 43 ref.

Document Type: P (Serial) ; A (Analytic)

Country of Publication: United Kingdom

Language: English

Conjugate %%%vaccines%%% were prepared with S. aureus type 8 capsular %%%polysaccharide%%% (CP) using three carrier proteins : Pseudomonas aeruginosa exotoxin A (ETA), a non-toxic recombinant ETA (rEPA), and diphtheria toxoid (DTd). Adipic acid dihydrazide (ADH) or N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) was used as a spacer to link the CP to carrier protein. All conjugates gave a high immune response with a boost after the second immunization. Conjugates prepared with ADH gave higher antibody titers than conjugates prepared with SPDP. IgG SUB 1 was the primary subclass elicited by all conjugates regardless of the carrier protein or the conjugation method used to prepare the %%%vaccines%%%. The non-immunogenic CP and the conjugates were formulated with either monophosphoryl lipid A (MPL), QS21, or in Novasomes and evaluated in mice. While the adjuvants failed to improve the immunogenicity of the nonconjugated CP, a more than fivefold increase in the antibody levels was observed when these adjuvants were used with the conjugates. Significant rises in IgG SUB 2 SUB b and IgG SUB 3 were observed with all formulations. The enhancement of the immunogenicity and the IgG subclass shift, as seen with some adjuvants, may prove to be important in %%%immunocompromised%%% patients.

7/7/53 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

02285162 SUPPLIER NUMBER: 110488906 (THIS IS THE FULL TEXT)

Primary immunodeficiencies.
Cooper, Megan A.; Pommering, Thomas L.; Koranyi, Katalin
American Family Physician, 68, 10, 2001
Nov 15,
2003

04605714 Genuine Article#: TW105 Number of References: 20
Title: %%%STAPHYLOCOCCAL%%% VACCINES - A REALISTIC DREAM
Author(s): FATTOM AI; NASO R
Corporate Source: UNIVAX BIOL INC,MICROBIAL PATHOGENESIS LAB,12280 WILKINS AVE/ROCKVILLE//MD/20852
Journal: ANNALS OF MEDICINE, 1996, V28, N1 (FEB), P43-46
ISSN: 0785-3890
Language: ENGLISH Document Type: ARTICLE
Abstract: %%%Staphylococcus%%% aureus, especially multidrug resistant strains, continues to be a leading cause of serious nosocomial infections. In spite of the debate among investigators in the field, the discovery of serologically distinct capsular polysaccharides on the surface of clinical isolates has renewed the prospects for development of vaccines and passive protective immunity against S. aureus infections. Capsular polysaccharide %%%conjugate%%% vaccines have now been produced and proven to be safe and immunogenic in both healthy and in a significant percentage of immunocompromised patients. Antibodies generated in humans against these vaccines have been shown to mediate type-specific opsonophagocytosis, and to protect animals against lethal challenge with the appropriate S. aureus isolate.

06518604 EMBASE No: 1996183313

Immunogenicity in mice of multivalent %%%conjugates%%% composed of %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides and alpha- and beta-toxins

Herbelin C.; Poutrel B.
Institut Nat Recherche Agronomique, Lab Pathologie Infectieuse Immunol,37380 Nouzilly France

Vaccine Research (VACCINE RES.) (United States) 1996, 5/1 (15-28)
CODEN: VAREE ISSN: 1056-7909
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Preparation of vaccines composed of sonicated %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides (CP5 and CP8), respectively, bound to alpha- and beta-toxins is described. Antibody responses in adult OF1 mice after subcutaneous injection of each %%%conjugate%%% (divalent %%%conjugates%%%, noted CP5~alpha and CP8~beta %%%conjugates%%%) or a mixture of the two %%%conjugates%%% (multivalent %%%conjugates%%%) were evaluated. Type-specific antibodies to CP5 and CP8 were elicited and the levels of antibodies were similar when mice received one of each %%%conjugate%%% or multivalent %%%conjugates%%%. Antibody responses to CPs were dose dependent and were enhanced after carrier priming with alpha- and beta-toxins. Multiple injections stimulated booster responses to CPs and toxins. Serum from mice immunized with %%%conjugates%%% also neutralized hemolytic activities induced in vitro by the native alpha- and beta-toxins.

12442231 PASCAL No.: 96-0099021

Effect of %%%conjugation%%% methodology, carrier protein, and adjuvants on the immune response to Staphyloccus aureus capsular polysaccharides

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Journal: Vaccine, 1995, 13 (14) 1288-1293

ISSN: 0264-410X CODEN: VACCDE Availability: INIST-20289; 354000055561550030

No. of Refs.: 43 ref.

Document Type: P (Serial) ; A (Analytic)

Country of Publication: United Kingdom

Language: English

%%%Conjugate%%% vaccines were prepared with S. aureus %%%type%%% %%%8%%% capsular polysaccharide (CP) using three carrier proteins : Pseudomonas aeruginosa exotoxin A (ETA), a non-toxic recombinant ETA (rEPA), and diphtheria toxoid (DTd). Adipic acid dihydrazide (ADH) or N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) was used as a spacer to link the CP to carrier protein. All %%%conjugates%%% gave a high immune response with a boost after the second immunization. %%%Conjugates%%% prepared with ADH gave higher antibody titers than %%%conjugates%%% prepared with SPDP. IgG SUB 1 was the primary subclass elicited by all %%%conjugates%%% regardless of the carrier protein or the %%%conjugation%%% method used to prepare the vaccines. The non-immunogenic CP and the %%%conjugates%%% were formulated with either monophosphoryl lipid A (MPL), QS21, or in Novasomes and evaluated in mice. While the adjuvants failed to improve the immunogenicity of the nonconjugated CP, a more than fivefold increase in the antibody levels was observed when these adjuvants were used with the %%%conjugates%%% . Significant rises in IgG SUB 2 SUB b and IgG SUB 3 were observed with all formulations. The enhancement of the immunogenicity and the IgG subclass shift, as seen with some adjuvants, may prove to be important in immunocompromised patients.

136068701 CA: 136(5)68701m PATENT
Multi-valent capsular polysaccharide vaccines
INVENTOR(AUTHOR): Boutriau, Dominique; Capiau, Carine; Desmons, Pierre Michel; Lemoine, Dominique; Poolman, Jan
LOCATION: Belg.
ASSIGNEE: Smithkline Beecham Biologicals S.A.
PATENT: PCT International ; WO 200200249 A2 DATE: 20020103
APPLICATION: WO 2001EP7288 (20010627) *GB 200015999 (20000629) *GB 20018363 (20010403) *GB 20018364 (20010403)
PAGES: 31 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/00A
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
SECTION:
CA215002 Immunochemistry

0013581397 BIOSIS NO.: 200200174908
Use of a %%%Staphylococcus%%% aureus %%%conjugate%%% vaccine in patients receiving hemodialysis
AUTHOR: Shinefield Henry (Reprint); Black Steven; Fattom Ali; Horwith Gary; Rasgon Scott; Ordonez Juan; Yeoh Hock; Law David; Robbins John B; Schneerson Rachel; Muenz Larry; Naso Robert
AUTHOR ADDRESS: Kaiser Permanente Vaccine Study Center, 1 Kaiser Plaza, 16th Fl., Oakland, CA, 94612, USA**USA
JOURNAL: New England Journal of Medicine 346 (7): p491-496 February 14, 2002 2002
MEDIUM: print
ISSN: 0028-4793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: In patients with decreased resistance to infection, %%%Staphylococcus%%% aureus is a major cause of bacteremia and its complications. The capsular polysaccharides are essential for the pathogenesis of and immunity to S. aureus infection and are targets for vaccines. Methods: In a double-blind trial involving patients with end-stage renal disease who were receiving hemodialysis, we evaluated the safety, immunogenicity, and efficacy of a vaccine with S. aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides %%%conjugated%%% to nontoxic recombinant Pseudomonas aeruginosa exotoxin A. Between April 1998 and August 1999, 1804 adult patients at 73 hemodialysis centers were randomly assigned to receive a single intramuscular injection of either vaccine or saline. IgG antibodies to S. aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides were measured for up to two years, and episodes of S. aureus bacteremia were recorded. Efficacy was estimated by comparing the incidence of S. aureus bacteremia in the patients who received the vaccine with the incidence in the control patients. Results: Reactions to the vaccine were generally mild to moderate, and most resolved within two days. The capsular polysaccharides elicited an antibody response of at least 80 mug per milliliter (the estimated minimal level conferring protection) in 80 percent of patients for %%%type%%% %%%5%%% and in 75 percent of patients for %%%type%%% %%%8%%%. The efficacy during weeks 3 to 54 was only 26 percent (P=0.23). However, between weeks 3 and 40 after vaccination, S. aureus bacteremia developed in 11 of 892 patients in the vaccine group who could be evaluated for bacteremia, as compared with 26 of 906 patients in the control group (estimate of efficacy, 57 percent; 95 percent confidence interval, 10 to 81 percent; nominal P=0.02). Conclusions: In patients receiving hemodialysis, a %%%conjugate%%% vaccine can confer partial immunity against S. aureus bacteremia for approximately 40 weeks, after which protection wanes as antibody levels decrease.

3/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013202688 BIOSIS NO.: 200100374527
%%%Staphylococcus%%% aureus capsular polysaccharide %%%type%%% %%%5%%% %%%conjugate%%% and whole cell vaccines stimulate antibody responses in cattle
AUTHOR: Tollersrud Tore (Reprint); Zernichow Lillian; Andersen Svein Rune;

Kenny Kevin; Lund Arve
AUTHOR ADDRESS: Department of Immunoprophylaxis, National Veterinary Institute, 0033, Oslo, Norway**Norway
JOURNAL: Vaccine 19 (28-29): p3896-3903 16 July, 2001 2001
MEDIUM: print
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Dairy heifers were immunized subcutaneously with one of four different vaccines which contained preparations of %%%Staphylococcus%%% aureus capsular polysaccharide %%%type%%% %%%5%%% (CP5) and a mineral oil adjuvant, or received a placebo containing saline and adjuvant. The vaccine containing a CP5-human serum albumin %%%conjugate%%% (CP5-HSA) and the vaccine with formaldehyde inactivated whole cells expressing CP5, both elicited strong anti-CP5 antibody responses. After two injections three weeks apart and a third injection 10 months later, the mean level and duration of the anti-CP5 antibody response was significantly higher in the whole cell group. No differences were found between the two groups with regard to the relative proportion of IgG subclasses, and the antibody responses to the polysaccharide were composed of both the IgG1 and IgG2. Vaccines containing only free CP5 or CP5 mixed with HSA produced weak and transient humoral immune responses. Only animals vaccinated with the whole cell vaccine or the %%%conjugate%%% vaccine showed responses to CP5 in a lymphocyte proliferation assay conducted one year after the third vaccination. This study indicates that CP5 expressed on the surface of formaldehyde inactivated whole cells, emulsified in an oil adjuvant, gives a strong and long lasting immune response in cattle. The use of %%%conjugation%%% technology, although effective, might not be necessary in order to achieve an immune response against S. aureus CP5 in cattle.

0013581397 BIOSIS NO.: 200200174908
Use of a %%%Staphylococcus%%% aureus %%%conjugate%%% vaccine in patients receiving hemodialysis
AUTHOR: Shinefield Henry (Reprint); Black Steven; Fattom Ali; Horwith Gary; Rasgon Scott; Ordonez Juan; Yeoh Hock; Law David; Robbins John B; Schneerson Rachel; Muenz Larry; Naso Robert
AUTHOR ADDRESS: Kaiser Permanente Vaccine Study Center, 1 Kaiser Plaza, 16th Fl., Oakland, CA, 94612, USA**USA
JOURNAL: New England Journal of Medicine 346 (7): p491-496 February 14, 2002 2002
MEDIUM: print
ISSN: 0028-4793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: In patients with decreased resistance to infection, %%%Staphylococcus%%% aureus is a major cause of bacteremia and its complications. The capsular polysaccharides are essential for the pathogenesis of and immunity to S. aureus infection and are targets for vaccines. Methods: In a double-blind trial involving patients with end-stage renal disease who were receiving hemodialysis, we evaluated the safety, immunogenicity, and efficacy of a vaccine with S. aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides %%%conjugated%%% to nontoxic recombinant Pseudomonas aeruginosa exotoxin A. Between April 1998 and August 1999, 1804 adult patients at 73 hemodialysis centers were randomly assigned to receive a single intramuscular injection of either vaccine or saline. IgG antibodies to S. aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides were measured for up to two years, and episodes of S. aureus bacteremia were recorded. Efficacy was estimated by comparing the incidence of S. aureus bacteremia in the patients who received the vaccine with the incidence in the control patients. Results: Reactions to the vaccine were generally mild to moderate, and most resolved within two days. The capsular polysaccharides elicited an antibody response of at least 80 mug per milliliter (the estimated minimal level conferring protection) in 80 percent of patients for %%%type%%% %%%5%%% and in 75 percent of patients for %%%type%%% %%%8%%%. The efficacy during weeks 3 to 54 was only 26 percent (P=0.23). However, between weeks 3 and 40 after vaccination, S. aureus bacteremia developed in 11 of 892 patients in the vaccine group who could be evaluated for bacteremia, as compared with 26 of 906 patients in the control group (estimate of efficacy, 57 percent; 95 percent confidence interval, 10 to 81 percent; nominal P=0.02). Conclusions: In patients receiving hemodialysis, a %%%conjugate%%% vaccine can confer partial immunity against S. aureus bacteremia for approximately 40 weeks, after which protection wanes as antibody levels decrease.

0011754046 BIOSIS NO.: 199900013706
Epitopic overload at the site of injection may result in suppression of the immune response to combined capsular polysaccharide %%%conjugate%%% vaccines
AUTHOR: Fattom Ali (Reprint); Cho Yun Hee; Chu Chiayung; Fuller Steven; Fries Louis; Naso Robert
AUTHOR ADDRESS: Walter Karakawa Microbial Pathogenesis Lab., NABI, Rockville, MD 20852, USA**USA
JOURNAL: Vaccine 17 (2): p126-133 Jan., 1999 1999
MEDIUM: print
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Capsular polysaccharide (CP) %%%conjugate%%% vaccines targeting a variety of bacterial infections are currently under development and clinical evaluation. The inclusion of multiple CP serotypes combined in a single injection is an important maneuver being evaluated. The combination of CP %%%conjugate%%% vaccines into a single multivalent injection may result in competition among the different components and adversely affect the immunogenicity of any individual %%%conjugate%%%. We observed a reduction of 30-90% in antibody responses to several serotypes in mice when immunogenicity of a 12-valent Escherichia coli (E. coli) lipopolysaccharide (LPS) %%%conjugate%%% vaccine was compared to the immunogenicity of each monovalent vaccine evaluated separately. A reduction of 30% was observed in the %%%Staphylococcus%%% aureus (S. aureus) %%%type%%% %%%8%%% CP antibodies when a %%%type%%% %%%8%%%-rEPA %%%conjugate%%% was combined with a %%%type%%% %%%5%%%-rEPA %%%conjugate%%%. S. aureus types 5 and 8-rEPA %%%conjugates%%% were combined with 100 mug of either rEPA (homologous) or diphtheria toxoid (DT) (heterologous) carrier proteins, and evaluated in rEPA or DT primed mice. The addition of the homologous protein resulted in a 64% reduction in %%%type%%% %%%5%%% CP antibodies. The heterologous protein did not affect the immunogenicity of the %%%type%%% %%%5%%%. We postulate that the free protein competed with the %%%conjugate%%% and recruited most of the rEPA primed T cells. In the case of the DT %%%conjugates%%%, the DT targeted different populations of the T cells, thus interference was not observed. These data suggested that the epitopic load rather than the antigenic load at the site of injection caused reduced immunogenicity of the %%%conjugates%%%. We theorize that individual components of multivalent CP vaccines %%%conjugated%%% to the same carrier proteins would compete for a limited number of specific carrier protein primed T cells. This would result in one or more components being unavailable in eliciting a sufficient immune response. The use of multiple carrier proteins should be considered as an approach to reduce interference when multivalent %%%conjugate%%% vaccines are to be formulated into a single injection.

3/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011686347 BIOSIS NO.: 199800480594
Antigenic determinants of %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% and %%%type%%% %%%8%%% capsular polysaccharide vaccines
AUTHOR: Fattom Ali I (Reprint); Sarwar Jawad; Basham Lisa; Ennifar Sofiane; Naso Robert
AUTHOR ADDRESS: Nabi, 12280 Wilkins Ave., Rockville, MD 20852, USA**USA
JOURNAL: Infection and Immunity 66 (10): p4588-4592 Oct., 1998 1998
MEDIUM: print
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Bacterial capsular polysaccharides (CP) are carbohydrate polymers comprised of repeating saccharide units. Several of these CP have side chains attached to their backbone structures. The side chains may include O-acetyl, phosphate, sialic acid, and other moieties. Those moieties represent the immunodominant epitopes and the most functional ones. The clinically significant %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% CP (CP 5) and %%%type%%% %%%8%%% CP (CP 8) are comprised of a trisaccharide repeat unit with one O-acetyl group attached to each repeat unit. The immunogenicity of these CP and the functionality of antibodies to the backbone and the O-acetyl moieties were investigated. Immunization with the native CP %%%conjugates%%% (CP with 75% O-acetylation) elicited a high proportion of antibodies directed against the O-acetyl moiety. Nonetheless, all of the vaccines produced antibodies to the backbone moieties as well. %%%Conjugate%%% vaccines made of de-O-acetylated CP elicited backbone antibodies only. Antibodies to both backbone and O-acetyl groups were found to be opsonic against S. aureus strains which varied in their O-acetyl content. Absorption studies with O-acetylated and de-O-acetylated CP showed that (i) native CP %%%conjugates%%% generated antibodies to both backbone and O-acetyl groups and (ii) O-acetylated isolates were opsonized by both populations of antibodies while the non-O-acetylated strains were predominantly opsonized by the backbone antibodies. These results suggest that S. aureus CP %%%conjugate%%% vaccines elicit multiple populations of antibodies with diverse specificities. Moreover, the antibodies of different specificities (backbone or O-acetyl) are all functional and efficient against the variations in bacterial CP that may occur among clinically significant S. aureus pathogenic isolates.

0010356694 BIOSIS NO.: 199698824527
A %%%Staphylococcus%%% aureus capsular polysaccharide (CP) vaccine and CP-specific antibodies protect mice against bacterial challenge
AUTHOR: Fattom Ali I (Reprint); Sarwar Jawad; Ortiz Alberto; Naso Robert
AUTHOR ADDRESS: W. W. Karakawa Microbial Pathogenesis Laboratory, NABI-Rockville, 12280 Wilkins Ave., Rockville, MD 20852, USA**USA
JOURNAL: Infection and Immunity 64 (5): p1659-1665 1996 1996
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The efficacy of capsular polysaccharide (CP)-specific antibodies elicited by active immunization with vaccines composed of %%%Staphylococcus%%% aureus types 5 and 8 CP linked to Pseudomonas aeruginosa exoprotein A or with immune immunoglobulin G (I-IgG) obtained from vaccinated plasma donors was tested in lethal and sublethal bacterial mouse challenge models. A dose of 2 times 10-5 CFU of S. aureus %%%type%%% %%%5%%% CP per mouse administered intraperitoneally (i.p.) with 5% hog mucin was found to cause 80 to 100% mortality in BALB/c mice within 2 to 5 days. Mice passively immunized i.p. 24 h earlier or subcutaneously 48 h earlier with 0.5 ml of I-IgG showed significantly higher average survival rates than animals receiving standard IgG or saline (P lt 0.01) following the bacterial challenge. Animals actively immunized with the monovalent %%%type%%% %%%5%%% CP-P. aeruginosa exoprotein A %%%conjugate%%% showed a survival rate of 73% compared with 13% in phosphate-buffered saline-immunized animals. The prechallenge geometric mean titer of %%%type%%% %%%5%%% CP antibodies in animals that died was significantly (P lt 0.05) lower than that of animals which survived the challenge (95.7 versus 223.6 mu-g/ml, respectively). The IgG was further evaluated in mice challenged i.p. with a sublethal dose of 5 times 10-4 CFU per mouse. Serial blood counts were performed on surviving animals at 6, 12, 24, and 48 h. Surviving animals were sacrificed at 72 h, and bacterial counts were performed on their kidneys, livers, and peritoneal lavage fluids. Animals receiving I-IgG had lower bacterial counts in blood samples and lower bacterial densities in kidneys, livers, and peritoneal lavage samples than mice immunized with standard IgG (P lt 0.05). These data suggest that S. aureus %%%type%%% %%%5%%% CP antibodies induced by active immunization or administered by passive immunization confer protection against S. aureus infections.

3/7/24 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

06518604 EMBASE No: 1996183313

Immunogenicity in mice of multivalent %%%conjugates%%% composed of %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides and alpha- and beta-toxins

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Institut Nat Recherche Agronomique, Lab Pathologie Infectieuse Immunol,37380 Nouzilly France

Vaccine Research (VACCINE RES.) (United States) 1996, 5/1 (15-28)
CODEN: VAREE ISSN: 1056-7909
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Preparation of vaccines composed of sonicated %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides (CP5 and CP8), respectively, bound to alpha- and beta-toxins is described. Antibody responses in adult OF1 mice after subcutaneous injection of each %%%conjugate%%% (divalent %%%conjugates%%%, noted CP5~alpha and CP8~beta %%%conjugates%%%) or a mixture of the two %%%conjugates%%% (multivalent %%%conjugates%%%) were evaluated. Type-specific antibodies to CP5 and CP8 were elicited and the levels of antibodies were similar when mice received one of each %%%conjugate%%% or multivalent %%%conjugates%%%. Antibody responses to CPs were dose dependent and were enhanced after carrier priming with alpha- and beta-toxins. Multiple injections stimulated booster responses to CPs and toxins. Serum from mice immunized with %%%conjugates%%% also neutralized hemolytic activities induced in vitro by the native alpha- and beta-toxins.

03885578 NLM Doc No: CRISP/96/HD01301-13 Sec. Source ID: CRISP/96/HD01301-13

HUMAN IMMUNE RESPONSE TO POLYSACCHARIDE-PROTEIN %%%CONJUGATE%%% VACCINES

SCHNEERSON R
NICHD, NIH

Source: Crisp Data Base National Institutes Of Health
Pub. Year: 1995
Sponsoring Agency: U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
Award Type: Intramural Project
Document type: Research
Languages: ENGLISH
Record type: Completed

RPROJ The surface polysaccharides of bacterial pathogens, which include capsular polysaccharides and lipopolysaccharides, serve as protective antigens. The immunologic properties of these bacterial polysaccharides, namely their age-related and T-cell independent immunogenicity, limit their use as vaccines. Covalently attachment to medically-useful proteins to form %%%conjugates%%% , both increases their immunogenicity and confers T-cell dependent properties to these polysaccharides. The capsular polysaccharides of Streptococcus pneumococcus type 6B, %%%Staphylococcus%%% aureus types 5 and 8, Group B streptococcus type 3 have been bound to several proteins and evaluated clinically. S. aureus %%%type%%% %%%5%%%-rEPA was evaluated in end stage renal disease patients; %%%type%%% %%%5%%% antibodies of the three major Ig classes rose significantly though to a lesser degree than in healthy volunteers, no booster response to reinjection at 6 weeks was found. These antibodies had opsonophagocytic activities. Pn6B-TT was evaluated in patients with sickle cell disease, healthy infants at 3, 4 and 6 months of age or at 7 and 9 months of age. Type specific antibodies of the three Ig classes, with booster responses, were induced. The magnitude of these responses was lesser than of Hib- TT. GBSIII-TT was evaluated in females of child bearing age. IgG antitype III rose similarly to the response to the polysaccharide alone. Technical problems with this lot were identified. All %%%conjugates%%% were safe, with only minor local reaction. The LPS of shigellae was detoxified, their O-specific polysaccharides bound to bacterial toxoids and their immunogennicity in mice found to be satisfactory. In Phase 1 and Phase 2 studies, these %%%conjugates%%% of the O-specific polysaccharides were safe and immunogenic: LPS antibody levels elicited by the investigational %%%conjugates%%% were similar to those in recruits convalescent from shigellosis. In preliminary studies, a S. sonnei-rEPA %%%conjugate%%% protected against shigellosis caused by this pathogen. A more extensive study showed protection of 75%.

Record Date Created: 199604

0014388995 BIOSIS NO.: 200300347714
In vivo production of capsular polysaccharide (CP) production as evidenced by type specific antibody increase following %%%Staphylococcus%%% aureus (SA) bacteremia in hemodialysis patients.
AUTHOR: Fattom A I (Reprint); Wu Y (Reprint); Propst M (Reprint); Fuller S (Reprint); Horwith G (Reprint); Naso R (Reprint)
AUTHOR ADDRESS: Nabi Biopharmaceuticals, Rockville, MD, USA**USA
JOURNAL: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy 42 p238 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy San Diego, CA, USA September 27-30, 2002; 20020927
SPONSOR: American Society for Microbiology
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

0014309114 BIOSIS NO.: 200300277833
Serotyping of %%%Staphylococcus%%% aureus (SA) bacteremia isolates and their in vitro opsonophagocytic killing mediated by antibodies specific to %%%type%%% %%%5%%% (T5), %%%type%%% %%%8%%% (T8) and 336 polysaccharides (PS).
AUTHOR: Gupte A (Reprint); Wu Y (Reprint); Propst M (Reprint); Fiore C (Reprint); Roghmann M; Johnson J; Edelman R; Taylor K (Reprint); Fattom A (Reprint)
AUTHOR ADDRESS: Nabi Biopharmaceuticals, Rockville, MD, USA**USA
JOURNAL: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy 42 p32 2002 2002
MEDIUM: print
CONFERENCE/MEETING: American Society for Microbiology (ASM) Annual Meeting on Infectious Disaease San Diego, CA, USA September 27-30, 2002; 20020927
SPONSOR: American Society for Microbiology
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

0014246173 BIOSIS NO.: 200300204892
%%%Staphylococcus%%% aureus antigen-containing whole cell %%%vaccine%%%
AUTHOR: Fattom Ali Ibrahim (Reprint)
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1268 (4): Mar. 25, 2003 2003
MEDIUM: e-file
ISSN: 0098-1133 _(ISSN print)
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A negatively-charged S. aureus antigen contains beta-hexosamine as a major carbohydrate component. S. aureus strains that carry the antigen account for nearly all of the clinically significant strains of S. aureus that are not %%%Type%%% %%%5%%% or %%%Type%%% %%%8%%% strains. The antigen can be used in combination with S. aureus %%%Type%%% %%%5%%% polysaccharide antigen and S. aureus %%%Type%%% %%%8%%% polysaccharide antigen to provide nearly 100% coverage of S. aureus infection. The antigen and antibodies to the antigen are useful in kits and assays for diagnosing S. aureus infection. A whole cell %%%vaccine%%% of cells that contain the antigen is particularly useful in the treatment of mastitis.

0013581397 BIOSIS NO.: 200200174908
Use of a %%%Staphylococcus%%% aureus conjugate %%%vaccine%%% in patients receiving hemodialysis
AUTHOR: Shinefield Henry (Reprint); Black Steven; Fattom Ali; Horwith Gary; Rasgon Scott; Ordonez Juan; Yeoh Hock; Law David; Robbins John B; Schneerson Rachel; Muenz Larry; Naso Robert
AUTHOR ADDRESS: Kaiser Permanente Vaccine Study Center, 1 Kaiser Plaza, 16th Fl., Oakland, CA, 94612, USA**USA
JOURNAL: New England Journal of Medicine 346 (7): p491-496 February 14, 2002 2002
MEDIUM: print
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ABSTRACT: Background: In patients with decreased resistance to infection, %%%Staphylococcus%%% aureus is a major cause of bacteremia and its complications. The capsular polysaccharides are essential for the pathogenesis of and immunity to S. aureus infection and are targets for %%%vaccines%%%. Methods: In a double-blind trial involving patients with end-stage renal disease who were receiving hemodialysis, we evaluated the safety, immunogenicity, and efficacy of a %%%vaccine%%% with S. aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides conjugated to nontoxic recombinant Pseudomonas aeruginosa exotoxin A. Between April 1998 and August 1999, 1804 adult patients at 73 hemodialysis centers were randomly assigned to receive a single intramuscular injection of either %%%vaccine%%% or saline. IgG antibodies to S. aureus %%%type%%% %%%5%%% and 8 capsular polysaccharides were measured for up to two years, and episodes of S. aureus bacteremia were recorded. Efficacy was estimated by comparing the incidence of S. aureus bacteremia in the patients who received the %%%vaccine%%% with the incidence in the control patients. Results: Reactions to the %%%vaccine%%% were generally mild to moderate, and most resolved within two days. The capsular polysaccharides elicited an antibody response of at least 80 mug per milliliter (the estimated minimal level conferring protection) in 80 percent of patients for %%%type%%% %%%5%%% and in 75 percent of patients for %%%type%%% %%%8%%%. The efficacy during weeks 3 to 54 was only 26 percent (P=0.23). However, between weeks 3 and 40 after %%%vaccination%%%, S. aureus bacteremia developed in 11 of 892 patients in the %%%vaccine%%% group who could be evaluated for bacteremia, as compared with 26 of 906 patients in the control group (estimate of efficacy, 57 percent; 95 percent confidence interval, 10 to 81 percent; nominal P=0.02). Conclusions: In patients receiving hemodialysis, a conjugate %%%vaccine%%% can confer partial immunity against S. aureus bacteremia for approximately 40 weeks, after which protection wanes as antibody levels decrease.

0011686347 BIOSIS NO.: 199800480594
Antigenic determinants of %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% and %%%type%%% %%%8%%% capsular polysaccharide %%%vaccines%%%
AUTHOR: Fattom Ali I (Reprint); Sarwar Jawad; Basham Lisa; Ennifar Sofiane; Naso Robert
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JOURNAL: Infection and Immunity 66 (10): p4588-4592 Oct., 1998 1998
MEDIUM: print
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Bacterial capsular polysaccharides (CP) are carbohydrate polymers comprised of repeating saccharide units. Several of these CP have side chains attached to their backbone structures. The side chains may include O-acetyl, phosphate, sialic acid, and other moieties. Those moieties represent the immunodominant epitopes and the most functional ones. The clinically significant %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% CP (CP 5) and %%%type%%% %%%8%%% CP (CP 8) are comprised of a trisaccharide repeat unit with one O-acetyl group attached to each repeat unit. The immunogenicity of these CP and the functionality of antibodies to the backbone and the O-acetyl moieties were investigated. Immunization with the native CP conjugates (CP with 75% O-acetylation) elicited a high proportion of antibodies directed against the O-acetyl moiety. Nonetheless, all of the %%%vaccines%%% produced antibodies to the backbone moieties as well. Conjugate %%%vaccines%%% made of de-O-acetylated CP elicited backbone antibodies only. Antibodies to both backbone and O-acetyl groups were found to be opsonic against S. aureus strains which varied in their O-acetyl content. Absorption studies with O-acetylated and de-O-acetylated CP showed that (i) native CP conjugates generated antibodies to both backbone and O-acetyl groups and (ii) O-acetylated isolates were opsonized by both populations of antibodies while the non-O-acetylated strains were predominantly opsonized by the backbone antibodies. These results suggest that S. aureus CP conjugate %%%vaccines%%% elicit multiple populations of antibodies with diverse specificities. Moreover, the antibodies of different specificities (backbone or O-acetyl) are all functional and efficient against the variations in bacterial CP that may occur among clinically significant S. aureus pathogenic isolates.

0011157144 BIOSIS NO.: 199799791204
Protective efficacy of antibodies to the %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% capsular polysaccharide in a modified model of endocarditis in rats
AUTHOR: Lee Jean C (Reprint); Park Jin-Sir; Shepherd Sara E; Carey Vincent; Fattom Ali
AUTHOR ADDRESS: Channing Lab., 181 Longwood Ave., Boston, MA 02115, USA** USA
JOURNAL: Infection and Immunity 65 (10): p4146-4151 1997 1997
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The protective efficacy of antibodies to the %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% capsular polysaccharide (CP5) was examined in a modified model of catheter-induced endocarditis. Rats were catheterized by surgically passing a polyethylene catheter through the right carotid artery and aortic valve into the left ventricle. The following day, the rats were injected by the intraperitoneal (i.p.) route with immunoglobulin G (IgG) purified from nonimmunized rabbits or from rabbits immunized with a conjugate %%%vaccine%%% composed of CP5 and CP8 linked covalently to recombinant Pseudomonas aeruginosa exotoxoid A. One day after passive immunization, the animals were challenged i.p. with one of three serotype 5 S. aureus isolates (strain Reynolds, Lowenstein, or VP) or nontypeable strain 521. Protection was evaluated by comparing quantitative cultures of blood, endocardial vegetations, and kidneys from control and immune animals. For experiments performed with S. aureus Reynolds and Lowenstein, rats given capsular antibodies (645 mu-g of CP5-specific IgG) showed a significantly (P lt 0.05) lower prevalence of endocarditis than rats injected with nonimmune IgG. Similarly, quantitative cultures of the blood, kidneys, and aortic valve vegetations revealed that fewer S. aureus cells were recovered from rats given capsule-specific IgG than from rats administered nonimmune IgG. Rats challenged with strain VP were protected with 1.145 mg of CP5-specific IgG. Capsular antibodies did not protect against infection elicited by a nontypeable strain. These results demonstrate that capsular antibodies elicited by immunization with a polysaccharide-protein conjugate %%%vaccine%%% protect experimental animals against serotype 5 S. aureus infection in a modified model of endocarditis.

0010356694 BIOSIS NO.: 199698824527
A %%%Staphylococcus%%% aureus capsular polysaccharide (CP) %%%vaccine%%% and CP-specific antibodies protect mice against bacterial challenge
AUTHOR: Fattom Ali I (Reprint); Sarwar Jawad; Ortiz Alberto; Naso Robert
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JOURNAL: Infection and Immunity 64 (5): p1659-1665 1996 1996
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The efficacy of capsular polysaccharide (CP)-specific antibodies elicited by active immunization with %%%vaccines%%% composed of %%%Staphylococcus%%% aureus types 5 and 8 CP linked to Pseudomonas aeruginosa exoprotein A or with immune immunoglobulin G (I-IgG) obtained from %%%vaccinated%%% plasma donors was tested in lethal and sublethal bacterial mouse challenge models. A dose of 2 times 10-5 CFU of S. aureus %%%type%%% %%%5%%% CP per mouse administered intraperitoneally (i.p.) with 5% hog mucin was found to cause 80 to 100% mortality in BALB/c mice within 2 to 5 days. Mice passively immunized i.p. 24 h earlier or subcutaneously 48 h earlier with 0.5 ml of I-IgG showed significantly higher average survival rates than animals receiving standard IgG or saline (P lt 0.01) following the bacterial challenge. Animals actively immunized with the monovalent %%%type%%% %%%5%%% CP-P. aeruginosa exoprotein A conjugate showed a survival rate of 73% compared with 13% in phosphate-buffered saline-immunized animals. The prechallenge geometric mean titer of %%%type%%% %%%5%%% CP antibodies in animals that died was significantly (P lt 0.05) lower than that of animals which survived the challenge (95.7 versus 223.6 mu-g/ml, respectively). The IgG was further evaluated in mice challenged i.p. with a sublethal dose of 5 times 10-4 CFU per mouse. Serial blood counts were performed on surviving animals at 6, 12, 24, and 48 h. Surviving animals were sacrificed at 72 h, and bacterial counts were performed on their kidneys, livers, and peritoneal lavage fluids. Animals receiving I-IgG had lower bacterial counts in blood samples and lower bacterial densities in kidneys, livers, and peritoneal lavage samples than mice immunized with standard IgG (P lt 0.05). These data suggest that S. aureus %%%type%%% %%%5%%% CP antibodies induced by active immunization or administered by passive immunization confer protection against S. aureus infections.

0008807510 BIOSIS NO.: 199395109776

Laboratory and clinical evaluation of conjugate %%%vaccines%%% composed of %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% and %%%type%%% %%%8%%% capsular polysaccharides bound to Pseudomonas aeruginosa recombinant exoprotein A

AUTHOR: Fattom Ali; Schneerson Rachel (Reprint); Watson Douglas C; Karakawa Walter W; Fitzgerald David; Pastan Ira; Li Xiuru; Shiloach Joseph; Bryla Dolores A; Robbins John B

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JOURNAL: Infection and Immunity 61 (3): p1023-1032 1993

ISSN: 0019-9567

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

0007266689 BIOSIS NO.: 199090051168
SYNTHESIS AND IMMUNOLOGIC PROPERTIES IN MICE OF %%%VACCINES%%% COMPOSED OF %%%STAPHYLOCOCCUS%%%-AUREUS %%%TYPE%%% %%%5%%% AND %%%TYPE%%% %%%8%%% CAPSULAR POLYSACCHARIDES CONJUGATED TO PSEUDOMONAS-AERUGINOSA EXOTOXIN A
AUTHOR: FATTOM A (Reprint); SCHNEERSON R; SZU S C; VANN W F; SHILOACH J; KARAKAWA W W; ROBBINS J B
AUTHOR ADDRESS: NATL INST CHILD HEALTH HUM DEV, BETHESDA, MD 20892, USA** USA
JOURNAL: Infection and Immunity 58 (7): p2367-2374 1990
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Epidemiological, serological and in vitro phagocytosis experiments provide that the newly discovered %%%type%%% %%%5%%% and %%%type%%% %%%8%%% capsular polysaccharides (CPs) are both virulence factors and protective antigens for bacteremia caused by %%%Staphylococcus%%% aureus. Neither %%%type%%% %%%5%%% nor %%%type%%% %%%8%%% CP elicited serum antibodies when injected into mice. These two CPs were found to Pseudomonas aeruginosa exotoxin A (ETA) to form conjugates by using the synthetic scheme devised for the CP (Vi) of Salmonella typhi and of pneumococcus type 12F (A. Fattom, W.F. Vann, S.C. Szu, A. Sutton, X. Li, D. Bryla, G. Schiffman, J.B. Robbins, and R. Schneerson, Infect. Immun. 56:2292-2298, 1988; S. C. Szu, A. L. Stone, J.D. Robbins, R. Schneerson, and J.B. Robbins, J. Exp. Med. 166:1510-1524, 1987). Both S. aureus CP-ETA conjugates elicited a rise in CP antibodies. As components of conjugates, both S. aureus CPs, acquired T-cell-dependent properties, as shown by their ability to respond to carrier priming and to stimulate booster responses. The conjugate-induced antibodies facilitated type-specific opsonization of S. aureus by human polymorphonuclear leukocytes. The conjugates also induced ETA antibodies which neutralized the native toxin in vitro. Clinical studies of these two conjugates for active or passive immunization of patients at risk for S. aureus bacteremia are planned.

04605714 Genuine Article#: TW105 Number of References: 20
Title: %%%STAPHYLOCOCCAL%%% %%%VACCINES%%% - A REALISTIC DREAM
Author(s): FATTOM AI; NASO R
Corporate Source: UNIVAX BIOL INC,MICROBIAL PATHOGENESIS LAB,12280 WILKINS AVE/ROCKVILLE//MD/20852
Journal: ANNALS OF MEDICINE, 1996, V28, N1 (FEB), P43-46
ISSN: 0785-3890
Language: ENGLISH Document Type: ARTICLE
Abstract: %%%Staphylococcus%%% aureus, especially multidrug resistant strains, continues to be a leading cause of serious nosocomial infections. In spite of the debate among investigators in the field, the discovery of serologically distinct capsular polysaccharides on the surface of clinical isolates has renewed the prospects for development of %%%vaccines%%% and passive protective immunity against S. aureus infections. Capsular polysaccharide conjugate %%%vaccines%%% have now been produced and proven to be safe and immunogenic in both healthy and in a significant percentage of immunocompromised patients. Antibodies generated in humans against these %%%vaccines%%% have been shown to mediate type-specific opsonophagocytosis, and to protect animals against lethal challenge with the appropriate S. aureus isolate.

03293644 H.W. WILSON RECORD NUMBER: BGSA96043644 (THIS IS THE FULLTEXT)
The biochemistry and genetics of capsular polysaccharide production in bacteria.
Roberts, Ian S
Annual Review of Microbiology v. 50 (1996) p. 285-315
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 14812

First Hit Fwd Refs

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L2: Entry 1 of 20 File: USPT Mar 9, 2004

DOCUMENT-IDENTIFIER: US 6703025 B1
TITLE: Multicomponent vaccines

Brief Summary Text (19):
Currently there is no FDA approved vaccine for the prevention of S. aureus infections. However, a S. aureus vaccine (StaphVAX), based on capsular polysaccharide, is currently being developed by NABI (North American Biologicals Inc.). This vaccine consists of type 5 or type 8 capsular polysaccharides conjugated to Pseudomonas aeruginosa exotoxin A (rEPA). The vaccine is designed to induce type-specific opsonic antibodies and enhance opsonophagocytosis (Karakawa et al., Infect Immun, 56:1090-1095, 1988). Using a refined lethal challenge mouse model (Fattom et al., Infect Immun, 61:1023-1032, 1993) it has been shown that intraperitoneal infusion of type 5 capsular polysaccharide specific IgG reduces the mortality of mice inoculated intraperitoneally with S. aureus. The type 5 capsular polysaccharide-rEPA vaccine has also been used to vaccinate seventeen patients with end-stage renal disease (Welch et al., J Amer Soc Nephrol, 7(2):247-253, 1996). Geometric mean (GM) IgG antibody levels to the type 5 conjugate increased between 13 and 17-fold after the first immunization, however no additional increases could be detected after additional injections. Interestingly, the GM IgM levels of the vaccinated patients were significantly lower than control individuals. Supported by the animal studies, the vaccine has recently completed a Phase II trial in continuous ambulatory peritorneal dialysis patients. The clinical trial showed the vaccine to be safe but ineffective in preventing staphylococcal infections (NABI SEC FORM 10-K405, Dec. 31, 1995). Two possible explanations for the inability of Staph VAX to prevent infections related to peritoneal dialysis in vaccinated patients are that the immunogenicity of the vaccine was too low due to suboptimal vaccine dosing or that antibodies in the bloodstream are unable to affect infection in certain anatomic areas, such as the peritoneum.

WEST Search History

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DATE: Monday, March 29, 2004

Hide?	Set Name	Query	Hit Count
		DB=USPT; PLUR=YES; OP=AND	
☐	L5	L3 and (immunocomprom$ or renal or elderly or neonate or surgery or immunosuppress$)	468
☐	L4	L3 and (immunocomprom$ or renal or elderly or neonate or surgery or immunosuppress$)	468
☐	L3	type and (5 or 8) and polysaccharide$ and (conjugate$ or glycoconjugate$) and staphylococc$	1111
☐	L2	L1 same staphylococc$	20
☐	L1	type same (5 or 8) same polysaccharide$ same (conjugate$ or glycoconjugate$)	111

END OF SEARCH HISTORY

First Hit

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L14: Entry 10 of 15 File: PGPB Oct 31, 2002

DOCUMENT-IDENTIFIER: US 20020159997 A1
TITLE: Staphylococcal immunotherapeutics via donor selection and donor stimulation

Abstract Paragraph:
A method and composition for the passive immunization of patients infected with or susceptible to infection from Staphylococcus bacteria such as S. aureus and S. epidermidis infection is provided that includes the selection or preparation of a donor plasma pool with high antibody titers to carefully selected Staphylococcus adhesins or MSCRAMMs, or fragments or components thereof, or sequences with substantial homology thereto. The donor plasma pool can be prepared by combining individual blood or blood component samples which have higher than normal titers of antibodies to one or more of the selected adhesins or other proteins that bind to extracellular matrix proteins, or by administering carefully selected proteins or peptides to a host to induce the expression of desired antibodies, and subsequently recovering the enhanced high titer serum or plasma pool from the treated host. In either case, the donor plasma pool is preferably purified and concentrated prior to intravenous introduction into the patient, and the present invention is advantageous in that a patient can be immunized against a wide variety of potentially dangerous staphylococcal infections. Kits for identifying potential donor with high titers of the selected adhesins are also provided. The present invention thus provides methods and compositions which can be highly effective against infections associated with Staphylococcus bacteria.

Summary of Invention Paragraph:
[0003] The staphylococci are Gram-positive spherical cells, usually arranged in grape-like irregular clusters. Some are members of the normal flora of the skin and mucous membranes of humans, others cause suppuration, abscess formation, a variety of pyogenic infections, and even fatal septicemia. Pathogenic staphylococci often hemolyze blood, coagulate plasma, and produce a variety of extracellular enzymes and toxins. The most common type of food poisoning is caused by a heat-stable staphylococci enterotoxin.

Summary of Invention Paragraph:
[0004] The genus Staphylococcus has at least 30 species. Three main species of clinical importance are Staphylococcus aureus, Staphylococcus epidermidis, and Staphylococcus haemolyticus. Staphylococcus aureus is coagulase-positive, which differentiates it from the other species. S. aureus is a major pathogen for humans. Almost every person has some type of S. aureus infection during a lifetime, ranging in severity from food poisoning or minor skin infections to severe life-threatening infections. The coagulase-negative staphylococci are normal human flora which sometimes cause infection, often associated with implanted devices, especially in very young, old and immunocompromised patients. Approximately 75% of the infections caused by coagulase-negative staphylococci are due to parasitic S. epidermidis. Infections due to Staphylococcus haemolyticus, Staphylococcus hominis, and other species are less common. S. saprophyticus is a relatively common cause of urinary tract infections in young women.

Summary of Invention Paragraph:
[0005] Staphylococcus bacteria such as S. aureus thus cause a spectrum of

infections that range from cutaneous lesions such as wound infections, impetigo, and furuncles to life-threatening conditions that include pneumonia, septic arthritis, sepsis, endocarditis, and biomaterial related infections. S. aureus colonization of the articular cartilage, of which collagen is a major component, within the joint space appears to be an important factor contributing to the development of septic arthritis. Hematogenously acquired bacterial arthritis remains a serious medical problem. This rapidly progressive and highly destructive joint disease is difficult to eradicate. Typically less than 50% of the infected patients failing to recover without serious joint damage. S. aureus is the predominant pathogen isolated from adult patients with hematogenous and secondary osteomyelitis.

Summary of Invention Paragraph:
[0006] In hospitalized patients, Staphylococcus aureus is a major cause of infection. Initial localized infections of wounds or indwelling medical devices can lead to more serious invasive infections such as septicemia, osteomyelitis, mastitis and endocarditis. In infections associated with medical devices, plastic and metal surfaces become coated with host plasma and matrix proteins such as fibrinogen and fibronectin shortly after implantation. The ability of Staphylococcus bacteria such as S. aureus to adhere to these proteins is essential to the initiation of infection. Vascular grafts, intravenous catheters, artificial heart valves, and cardiac assist devices are thrombogenic and prone to bacterial colonization. S. aureus is the most damaging pathogen of such infections, and other Staphylococci bacteria such as S. epidermidis are also responsible for a significant amount of dangerous infections, particularly those associated with implanted devices.

Summary of Invention Paragraph:
[0007] There is a strong and rapidly growing need for therapeutics to treat infections from Staphylococcus bacteria such as S. aureus and S. epidermidis infections which are effective against antibiotic resistant strains of the bacteria. The U.S. National Institutes for Health has recently indicated that this goal is now a national priority.

Summary of Invention Paragraph:
[0012] Supplemental immunoglobulin therapy has been shown to provide some measure of protection against certain encapsulated bacteria such as Hemophilus infuenzae and Streptococcus pneumoniae. Infants who are deficient in antibody are susceptible to infections from these bacteria and bacteremia and sepsis are common. When anti-Streptococcal and anti-Hemophilus antibodies are present, they provide protection by promoting clearance of the respective bacteria from the blood. In the case of antibody to Staphylococcus, the potential use of supplemental immunoglobulin to prevent or treat infection has been much less clear.

Summary of Invention Paragraph:
[0013] Early attempts to treat Staphylococcus infections focused on the potential use of supplemental immunoglobulin to boost peritoneal defenses, such as opsonic activity, in patients receiving continuous ambulatory peritoneal dialysis. Standard intravenous immunoglobulin (IVIG) was shown to have lot to lot variability for opsonic activity to S. epidermidis (L. A. Clark and C. S. F. Easmon, J. Clin. Pathol. 39:856 (1986)). In this study, one third of the IVIG lots tested had poor opsonization with complement, and only two of fourteen were opsonic without complement. Thus, despite the fact that the IVIG lots were made from large plasma donor pools, good opsonic antibody to S. epidermidis was not uniformly present. Moreover, this study did not examine whether IVIG could be used to prevent or treat S. epidermidis infections or bacterial sepsis.

Summary of Invention Paragraph:
[0014] Prior studies have associated coagulase-negative Staphylococcus bacteria, such as S. epidermidis, as the most common species causing bacteremia in neonates

receiving lipid emulsion infusion (Freeman, J. et al., N. Engl. J. Med. 323:301, 1990). These neonates had low levels of opsonic antibody to S. epidermidis despite the fact that the sera had clearly detectable levels of IgG antibodies to S. epidermidis peptidoglycan (Fleer, A. et al., J. Infect. Dis. 2:426, 1985). This was surprising because anti-peptidoglycan antibodies were presumed to be the principal opsonic antibodies. Thus, while suggesting that neonatal susceptibility to S. epidermidis might be related to impaired opsonic activity, these studies also suggested that many antibodies directed against S. epidermidis are not opsonic and would not be capable of providing protection when given passively to neonates.

Summary of Invention Paragraph:
[0016] Animal studies in the literature that demonstrated immunoglobulin protection against Staphylococcus infections have shown strain specificity by enzyme-linked immunosorbent assays (ELISA) and have utilized normal adult mice in protection studies. Animal models typically have used mature animals with normal immunity with unusually virulent strains or overwhelming-challenge doses of bacteria. Human patients are generally immunologically immature or debilitated. Human patients also get somewhat indolent infections with low virulence pathogens such as S. epidermidis with death usually attributable to secondary complications. Models that have used unusual strains or overwhelming bacterial doses, generally induce rapid fulminant death. These are important factors since antibodies generally work in concert with the host cellular immune system (neutrophils, monocytes, macrophages and fixed reticuloendothelial system). The effectiveness of antibody therapy may therefore be dependent on the functional immunologic capabilities of the host. To be predictive, animal models must closely emulate the clinical condition in which the infection would occur and capture the setting for therapy. Moreover, the animal studies have yielded inconsistent results.

Summary of Invention Paragraph:
[0017] One model has been reported which used an unusually virulent strain of S. epidermidis. Infected-mature mice developed 90 to 100% mortality within 24 to 48 hours (K. Yoshida et al., Japan. J. Microbiol. 20:209 (1976)). Antibody to S. epidermidis surface polysaccharide was protective in these mice. Protection was shown to occur with an IgM fraction, but not the IgG fraction (K. Yoshida and Y. Ichiman, J. Med. Microbiol 11:371 (1977)). This model, however, presents a pathology which is very different from that seen in typically infected patients. Intraperitoneally-challenged mice developed symptoms of sepsis within minutes of receiving the injection and died in 24 to 48 hours. This particular pathology is not observed in Staphylococcus infected humans. The highly virulent strain of S. epidermidis may represent an atypical type of infection. moreover, isolates of S. epidermidis from infected humans did not kill mice in this model.

Summary of Invention Paragraph:
[0022] U.S. Pat. No. 5,505,945 discloses compositions for passive immunity that contain a full repertoire of immunoglobulins, including IgA, IgM, and IgG to combat infections from microorganisms and viruses at wound, surgical, or bum sites. The compositions contain elevated antibody titers for several pathogens, including S. aureus, Coagulase Negative Staphylococci Enterococci, S. epidermidis, P. aeruginose, E. coli, and Enterobacter spp. However, these compositions are specifically designed to avoid the use of intravenous immunoglobulin or IVIG therapy, and instead are applied in the form of ointments, creams, sprays and the like which are designed for topical application only.

Summary of Invention Paragraph:
[0030] U.S. Pat. No. 5,571,511 describes the use of immunoglobulin from individual samples or pools of serum, plasma, whole blood, or tissue for the treatment of a Staphylococcus infection. Immunoglobulin is identified by performing a first assay to identify immunoglobulin which is reactive with a preparation of a first Staphylococcus organism, performing a second assay to identify immunoglobulin which is reactive with a preparation of a second Staphylococcus organism, and selecting

immunoglobulin which is reactive with the preparations from both the first and second Staphylococcus organisms. Reactivity is determined in immunological assays which may be binding assays, opsonization assays, or clearance assays. Preferably, the preparations of the first and the second Staphylococcus organisms are derived from different serotypes or different species, such as S. epidermidis and S. aureus, and more preferably, the first preparation is from S. epidermidis (Hay, ATCC 55133).

Summary of Invention Paragraph:
[0032] Accordingly, there still remains a need to provide more effective products and methods which make use of antibodies against MSCRAMMs and can be utilized in methods of intravenous immunoglobulin therapy so as to prevent and/or treat Staphylococcus infections, and preferably those that can exhibit a broad spectrum immunization against various strains of Staphylococcus bacteria.

Summary of Invention Paragraph:
[0036] Natural immunity to Staphylococcus infections remains poorly understood. Typically, healthy humans and animals exhibit a high degree of innate resistance to Staphylococcus bacteria such as S. aureus. Protection is attributed to intact epithelial and mucosal barriers and normal cellular and humoral responses. Titers of antibodies to S. aureus components are elevated after severe infections (Ryding et al., J. Med Microbiol, 43(5):328-334, 1995), however to date there is no serological evidence of a correlation between antibody titers and human immunity.

Summary of Invention Paragraph:
[0037] Over the past several decades live, heat-killed, and formalin fixed preparations of S. aureus cells have been tested as vaccines to prevent staphylococcal infections. A multicenter clinical trial was designed to study the effects of a commercial vaccine, consisting of a staphylococcus toxoid and whole killed staphylococci, on the incidence of peritonitis, exit site infection, and S. aureus nasal carriage among continuous peritoneal dialysis patients (Poole-Warren, L. A., et al., Clin Nephrol, 35:198-206, 1991). Although immunization with the vaccine elicited an increase in the level of specific antibodies to S. aureus, the incidence of peritonitis was unaffected. Similarly, immunization of rabbits with whole cells of S. aureus could not prevent or modify any stage in the development of experimental endocarditis, reduce the incidence of renal abscess, or lower the bacterial load in infected kidneys (Greenberg, D. P., et al., Infect Immun, 55:3030-3034, 1987).

Summary of Invention Paragraph:
[0038] Currently there is no FDA approved vaccine for the prevention of S. aureus infections. However, a S. aureus vaccine (StaphVAX), based on the capsular polysaccharide, is currently being developed by NABI (North American Biologicals Inc.). This vaccine consists of type 5 or type 8 capsular polysaccharides conjugated to Pseudomonas aeruginosa exotoxin A (rEPA). The vaccine is designed to induce type-specific opsonic antibodies and enhance opsonophagocytosis (Karakawa, W. W., et al., Infect Immun, 56:1090-1095, 1988). Using a refined lethal challenge mouse model (Fattom, A., et al., Infect Immun, 61:1023-1032, 1996) it has been shown that intraperitoneal infusion of type 5 specific IgG reduces the mortality of mice inoculated intraperitoneally with S. aureus. The type 5 capsular polysaccharide-rEPA vaccine has also been used to vaccinate seventeen patients with end-stage renal disease (Welch, et al., J Amer Soc Nephrol, 7(2):247-253, 1996). Geometric mean (GM) IgG antibody levels to the type 5 conjugate increased between 13 and 17-fold after the first immunization, however no additional increases could be detected after additional injections. Moreover, these vaccination regimens were not able to treat a variety of bacterial strains.

Summary of Invention Paragraph:
[0039] Interestingly, the GM IgM levels of the vaccinated patients were significantly lower than control individuals. Supported by the animal studies, the

vaccine has recently completed a Phase II trial in continuous ambulatory peritoneal dialysis patients. The clinical trial showed the vaccine to be safe but ineffective in preventing staphylococcal infections (NABI SEC FORM 10-K405, Dec. 31, 1995). Two possible explanations for the inability of StaphVAX to prevent infections related to peritoneal dialysis in vaccinated patients are that the immunogenicity of the vaccine was too low due to suboptimal vaccine dosing or that antibodies in the bloodstream are unable to affect infection in certain anatomic areas, such as the peritoneum.

Summary of Invention Paragraph:
[0042] A mouse mastitis model was used by Mamo, et al., in 1994 (Vaccine, 12:988-992) to study the effect of vaccination with fibrinogen binding proteins (especially FnBP-A) and collagen binding protein from S. aureus against challenge infection with S. aureus. The mice vaccinated with fibrinogen binding proteins showed reduced rates of mastitis compared with controls. Gross examination of challenged mammary glands of mice showed that the glands of mice immunized with fibrinogen binding proteins developed mild intramammary infection or had no pathological changes compared with glands from control mice. A significantly reduced number of bacteria could be recovered in the glands from mice immunized with fibrinogen binding proteins as compared with controls. Mamo then found that vaccination with FnBP-A combined with staphylococcal alpha toxoid did not improve the protection (Mamo, et al., Vaccine, 12:988-992, 1994). Next, Mamo, et al., immunized mice with only collagen binding protein, which did not induce protection against the challenge infection with S. aureus.

Summary of Invention Paragraph:
[0043] Whole killed staphylococci were included in a vaccine study in humans undergoing peritoneal dialysis (Poole-Warren, et al., Clinical Nephrology 35:198-206, 1991). In this clinical trial, a commercially available vaccine of alpha-hemolysin toxoid combined with a suspension of whole killed bacteria) was administered intramuscularly ten times over 12 months, with control patients receiving saline injections. Vaccination elicited significant increases in the levels of antibodies to S. aureus cells in the peritoneal fluid and to alpha-hemolysin in the serum. However, immunization did not reduce the incidences of peritonitis, catheter-related infections or nasal colonization among vaccine recipients. The lack of protective efficacy in this trial was attributed to a suboptimal vaccine formulation.

Summary of Invention Paragraph:
[0044] Secreted proteins have been explored as components of subcellular vaccines. The alpha toxin is among the most potent staphylococcal exotoxins; it has cytolytic activity, induces tissue necrosis and kills laboratory animals. Immunization with formaldehyde-detoxified alpha toxin does not protect animals from systemic or localized infections, although it may reduce the clinical severity of the infections (Ekstedt, R. D., The Staphylococci, 385-418, 1972)

Summary of Invention Paragraph:
[0045] One study has evaluated the protective efficacy of antibodies to the S. aureus microcapsule in an experimental model of staphylococcal infection (Nemeth, J. and Lee, J. C., Infect. Immun., 61:1023-1032, 1993). Rats were actively immunized with killed, microencapsulated bacteria or passively immunized with high-titer rabbit antiserum specific for the capsular polysaccharide. Control animals were injected with saline or passively immunized with normal rabbit serum. Protection against catheter-induced endocarditis resulting from intravenous challenge with the same strain was then evaluated. Despite having elevated levels of anticapsular antibodies, the immunized animals were susceptible to staphylococcal endocarditis and immunized and control animals had similar numbers of bacteria in the blood.

Summary of Invention Paragraph:

[0047] Despite the advances in the art of compositions for the treatment of infections from Staphylococcus bacteria such as S. aureus, there remains a need to provide a more effective product, and preferably one that exhibits a broad spectrum immunization against a variety of Staphylococcus bacterial strains. As described in the Detailed Description of the Invention, one approach to generating a prophylactic immunotherapeutic against bacteria is to stimulate donors with a vaccine containing a combination of MSCRAMMs. This approach of generating hyperimmune globulins can create a steady supply of plasma with high levels of the specific types of disease fighting antibodies. MSCRAMM hyperimmune globulins can be used to provide passive immunity against infection in neonates, trauma patients, immunocompromised patients or patients who are immediately at risk and do not have time to mount their own antibody response. Hyperimmune globulins have a high benefit-to-cost ratio, can be produced from a nonhuman or human source and have a high level of physician acceptance based on past usage.

Summary of Invention Paragraph:
[0048] Therefore, it is an object of the invention to provide new therapeutic compositions for active and passive immunization against Staphylococcus infections.

Summary of Invention Paragraph:
[0050] It is another object of the present invention to provide a therapeutic composition that immunizes against Staphylococcus bacteria such as S. aureus and S. epidermidis, increases the rate of opsonization and phagocytosis of a variety of Staphylococcus infections, and induces enhanced intracellular killing of Staphylococcus bacteria.

Summary of Invention Paragraph:
[0051] It is another object of the present invention to provide an immunological serum against staphylococci.

Summary of Invention Paragraph:
[0052] It is another object of the present invention to provide such a serum which yields humoral and cellular immunity against staphylococci.

Summary of Invention Paragraph:
[0053] It is another object of the present invention to provide such a serum which imparts short-term immunity against staphylococci.

Summary of Invention Paragraph:
[0054] It is a further object of the present invention to provide methods for detecting, diagnosing, treating, preventing or monitoring the progress of therapy for staphylococcal infections.

Summary of Invention Paragraph:
[0055] A method and composition for the passive immunization of patients infected with or susceptible to infection from Staphylococcus bacteria such as S. aureus and S. epidermidis infection is provided that includes the selection or preparation of a donor plasma pool with high antibody titers to carefully selected Staphylococcus adhesins or MSCRAMMs, or fragments or components thereof, or sequences with substantial homology thereto; purification, concentration, and treatment of the donor plasma pool as necessary to obtain immunoglobulin in a purified state that has a higher than normal antibody titer to the selected adhesins; and then administration of an effective amount of the purified immunoglobulin to the patient in need thereof. The donor plasma pool can be prepared, for example, by combining individual blood or blood component samples which have higher than normal titers of antibodies to one or more of the selected adhesins or other proteins that bind to extracellular matrix proteins, or fragments or sequences with substantial homology thereto, to produce the desired composite. Kits for the identification of donor plasma pools with high titers of the selected adhesins are also provided. In an

alternative embodiment, a method for obtaining a donor plasma pool that is highly effective against Staphylococcus bacterial infection is provided that includes administering carefully selected proteins or peptides to a host to induce the expression of desired antibodies, recovering the enhanced high titer serum or plasma pool from the host, optionally purifying and concentrating the immunoglobulin, and providing it to a patient in need thereof.

Detail Description Paragraph:
[0070] A method and composition for the passive immunization of patients infected with or susceptible to Staphylococcus bacterial infection, such as those caused by S. aureus or S. epidermidis, is provided that includes the selection or preparation of a donor plasma pool with high antibody titers to carefully selected Staphylococcus adhesins, or fragments thereof or sequences with substantial homology thereto; purification, concentration, and treatment of the donor plasma pool as necessary to obtain immunoglobulin in a purified state that has a higher than normal antibody titer to the selected staphylococcal adhesins; and then administration of an effective amount of the purified immunoglobulin to the patient in need thereof. The donor plasma pool can be prepared, for example by, by combining individual blood samples which have higher than normal titers of antibodies to one or more of the selected adhesins or fragments or sequences with substantial homology thereto. Kits for the identification of donor plasma pools with high titers of the selected adhesins are also provided. In an alternative embodiment, a method for obtaining a donor plasma pool that is highly effective against Staphylococcus infection is provided that includes administering carefully selected proteins or peptides to a host to induce the expression of desired antibodies, recovering the enhanced high titer plasma pool from the host, optionally purifying and concentrating the immunoglobulin, and providing it to a patient in need thereof.

Detail Description Paragraph:
[0084] The terms FnBP-A protein, FnBP-B protein, ClfA protein, ClfB protein, SdrC protein, SdrD protein, SdrE protein, CNA protein, EbpS protein and MHCII protein are defined herein to include FNBP-A, FNBP-B, ClfA, ClfB, SdrC, SdrD, SdrE, CNA, EbpS and MHCII subdomains, respectively, and active or antigenic fragments or components of FnBP-A, FnBP-B, ClFA, ClfB, SdrC, SdrD, SdrE, CNA, EbpS and MHCII proteins, respectively, or proteins or fragments having sufficiently high homology thereto. Active fragments or components of FnBP-A, FNBP-B, ClfA, ClfB, SdrC, SdrD, SdrE, CNA, EbpS and MHCII proteins are defined herein as peptides or polypeptides capable of blocking the binding of staphylococci bacteria to extracellular matrix proteins of the host. Antigenic fragments of FnBP-A, FnBP-B, ClfA, ClfB, SdrC, SdrD, SdrE, CNA, EbpS and MHCII proteins are defined herein as peptides or polypeptides capable of producing an immunological response.

Detail Description Paragraph:
[0101] As used herein, a "protective antibody" is an antibody which confers protection against infectious diseases caused by infection with staphylococci, when used to passively immunize an naive animal.

Detail Description Paragraph:
[0102] As used herein, a "protective epitope" is an epitope which is recognized by a protective antibody, and/or an epitope which, when used to immunize an animal, elicits an immune response sufficient to prevent or lessens the severity for some period of time, of any one of the disorders which can result from infection with staphylococci.

Detail Description Paragraph:
[0111] U.S. Pat. No. 5,440,014 discloses a fibronectin binding peptide within the D3 homology unit of a fibronectin binding protein of S. aureus which can be used for vaccination of ruminants against mastitis caused by staphylococcal infections, for treatment of wounds, for blocking protein receptors, for immunization of other

animals, or for use in a diagnostic assay.

Detail Description Paragraph:
[0116] Collagen is the major constituent of cartilage. Collagen (Cn) binding proteins are commonly expressed by staphylococcal strains. The Cn binding MSCRAMM of S. aureus adheres to cartilage in a process that constitutes an important part of the pathogenic mechanism in staphylococcal infections. (Switalski, et al. Mol. Micro. 7(1), 99-107, 1993) Cn binding by staphylococcal bacteria such as S. aureus is found to play a role in at least, but not only, arthritis and septicemia. CNA proteins with molecular weights of 133, 110 and 87 kDa (Patti, J., et al., J. Biol. Chem.,267:4766-4772, 1992) have been identified. Strains expressing CNAs with different molecular weights do not differ in their Cn binding ability (Switalski, L. M., et al., Mol. Microbiol., 7:99-107, 1993).

Detail Description Paragraph:
[0117] Staphylococcal strains recovered from the joints of patients diagnosed with septic arthritis or osteomyelitis almost invariably express a CNA, whereas significantly fewer isolates obtained from wound infections express this adhesin. (Switalski, L. M., et al., Mol. Microbiol., 7:99-107, 1993) Similarly, S. aureus strains isolated from the bones of patients with osteomyelitis more often have an MSCRAMM recognizing the bone-specific protein, bone sialoprotein (BSP) (Ryden, C., et al, Lancet, 11:515-518, 1987). S. aureus colonization of the articular cartilage within the joint space appears to be an important factor contributing to the development of septic arthritis.

Detail Description Paragraph:
[0138] PCT/US97/03106 discloses the gene sequences for an elastin binding protein. DNA sequence data disclosed indicates that the ebps open reading frame consists of 606 bp, and encodes a novel polypeptide of 202 amino acids. EbpS protein has a predicted molecular mass of 23,345 daltons and pI of 4.9. EbpS was expressed in E. coli as a fusion protein with polyhistidine residues attached to the N-terminus. A polyclonal antibody raised against recombinant EbpS interacted specifically with the 25 kDa cell surface EbpS and inhibited staphylococcal elastin binding. Furthermore, recombinant EbpS bound specifically to immobilized elastin and inhibited binding of Staphylococcus aureus to elastin. A degradation product of recombinant EbpS lacking the first 59 amino acids of the molecule and a C-terminal fragment of CNBr-cleaved recombinant EbpS, however, did not interact with elastin. These results strongly suggest that EbpS is the cell surface molecule mediating binding of Staphylococcus aureus to elastin. The finding that some constructs of recombinant EbpS do not interact with elastin suggests that the elastin binding site in EbpS is contained in the first 59 amino acids of the molecule.

Detail Description Paragraph:
[0141] Using overlapping EbpS fragments and recombinant constructs, the elastin binding site in EbpS was mapped to the amino terminal domain of the molecule (PCT/US97/03106). Overlapping synthetic peptides spanning amino acids 14-34 were then used to better define the binding domain. Among these, peptides corresponding to residues 14-23 and 18-34 specifically inhibited elastin binding by more than 95%. Common to all active synthetic peptides and proteolytic and recombinant fragments of EbpS is the hexameric sequence .sup.18Thr-Asn-Ser-His-Gln-Asp.sup.23. Further evidence that this sequence is important for elastin binding was the loss of activity when Asp.sup.23 was substituted with Asn in the synthetic peptide corresponding to residues 18-34. However, the synthetic hexamer TNSHQD by itself did not inhibit staphylococcal binding to elastin. These findings indicate that although the presence of the TNSHQD sequence is essential for EbpS activity, flanking amino acids in the N- or C-terminal direction and the carboxyl side chain of Asp.sup.23 are required for elastin recognition.

Detail Description Paragraph:
[0143] In addition to fibrinogen, fibronectin, collagen and elastin. S. aureus

strains associate with other adhesive eukaryotic proteins, many of which belong to the family of adhesive matrix proteins, such as vitronectin. (Chatwal, G. S., et al., Infect. Immun., 55:1878-1883, 1987). U.S. Pat. No. 5,648,240, incorporated herein by reference, discloses a DNA segment comprising a gene encoding a S. aureus broad spectrum adhesin that has a molecular weight of about 70 kDa. The adhesin is capable of binding fibronectin or vitronectin and includes a MHC II mimicking unit of about 30 amino acids. Further analyses of the binding specificities of this protein reveal that it functionally resembles an MHC II antigen in that it binds synthetic peptides. Thus, in addition to mediating bacterial adhesion to ECM proteins, it may play a role in staphylococcal infections by suppressing the immune system of the host. The patent further claims a recombinant vector that includes the specified DNA sequence, a recombinant host cell transformed with the vector, and DNA which hybridizes with the DNA of specified sequence. Also disclosed is a composition that includes a protein or polypeptide encoded by the specified DNA sequence and a method of inducing an immune response in an animal that includes administering an immunogenic composition that includes the encoded protein or polypeptide. A method of making a MHC II antigen protein analog comprising the steps of inserting the specified DNA sequence in a suitable expression vector and culturing a host cell transformed with the vector under conditions to produce the MHC II antigen protein analog is additionally claimed in the patent.

Detail Description Paragraph:
[0144] VII. SDR Proteins from Staphylococcus Epidermidis

Detail Description Paragraph:
[0145] Staphylococcus epidermidis, a coagulase-negative bacterium, is a common inhabitant of human skin and a frequent cause of foreign-body infections. Pathogenesis is facilitated by the ability of the organism to first adhere to, and subsequently to form biofilms on, indwelling medical devices such as artificial valves, orthopedic devices, and intravenous and peritoneal dialysis catheters. Device-related infections may jeopardize the success of medical treatment and significantly increase patient mortality. Accordingly, the ability to develop vaccines that can control or prevent outbreaks of S. epidermidis infection is of great importance, as is the development of means that can prevent or treat infection from a broad spectrum of bacteria, including both coagulase-positive and coagulase negative bacteria.

Detail Description Paragraph:
[0147] In accordance with the present invention, the donor selection and donor stimulation methods described herein can also be performed with regard to the SdrF, SdrG or an SdrH protein. In these methods, individuals may be identified and selected who have higher than normal antibody titers to the SdrF, SdrG or an SdrH proteins, and a donor plasma pool can be prepared which will have higher than normal titers to one or more of these proteins. Accordingly, donor plasma can be prepared in accordance with the present invention which will be useful in methods to prevent or treat infection from coagulase-negative staphylococcal infections such as those associated with S. epidermidis.

Detail Description Paragraph:
[0162] Using the peptide antigens described herein, the present invention also provides methods of stimulating high antibody levels in a donor, which includes administering to an animal, for example a human, a pharmaceutically-acceptable composition comprising an immunologically effective amount of an MSCRAMM-derived peptide composition. The composition can include partially or significantly purified MSCRAMM-derived peptide epitopes, obtained from natural or recombinant sources, which proteins or peptides may be obtainable naturally or either chemically synthesized, or alternatively produced in vitro from recombinant host cells expressing DNA segments encoding such epitopes. Smaller peptides that include reactive epitopes, such as those between about 30 and about 100 amino acids in length will often be preferred. The antigenic proteins or peptides may also be

combined with other agents, such as other staphylococcal or streptococcal peptide or nucleic acid compositions, if desired. The composition may also include staphylococcal produced bacterial components such as those discussed above, obtained from natural or recombinant sources, which proteins may be obtainable naturally or either chemically synthesized, or alternatively produced in vitro from recombinant host cells expressing DNA segments encoding such peptides.

Detail Description Paragraph:
[0168] The methods currently in use for plasma separation are centrifugation and filtration. The technique of U.S. Pat. No. 5,548,066 may be used to prepare the donor plasma pool if it is not commercially available, and is incorporated by reference herein. First, a plurality of blood donors are identified. These donors are mature mammals, typically mammals of the same species for which the serum will be employed. Where a specific ailment is to be treated or prevented, such as mastitis in mammals or other diseases caused by staphylococcal bacteria such as S. aureus, it is preferred that the donors have been exposed either naturally or through immunization to the causative organism or some antigenic portion thereof. Further, to achieve a consistent serum product, it is preferred that the donor group be relatively large. It is preferred to use human hosts to prepare the donor plasma pools. Once the donors have been identified, blood is drawn from the donors. Since the serum is refined directly from the blood, it is desired to obtain the maximum quantity of blood to thus obtain the maximum quantity of serum. For humans, an established limit of blood is drawn periodically over time.

Detail Description Paragraph:
[0198] The antibody obtained through this invention may be labeled directly with a detectable label for identification and quantification of staphylococcal bacterial such as S. aureus, S. epidermidis, etc. Labels for use in immunoassays are generally known to those skilled in the art and include enzymes, radioisotopes, and fluorescent, luminescent and chromogenic substances including colored particles such as colloidal gold and latex beads. Suitable immunoassays include enzyme-linked immunosorbent assays (ELISA).

Detail Description Paragraph:
[0213] The immunological compositions, such as vaccines, and other pharmaceutical compositions can be used alone or in combination with other blocking agents to protect against human and animal infections caused by staphylococcal bacterial including S. aureus and others. In particular, the compositions can be used to protect humans against endocarditis or to protect humans or ruminants against mastitis caused by staphylococcal infections. The vaccine can also be used to protect canine and equine animals against similar staphylococcal infections.

Detail Description Paragraph:
[0226] The invention includes a method for detecting biological samples with an elevated titer of antibodies to selected staphylococcal MSCRAMMs. As used herein the term biological sample refers to a sample of tissue or fluid isolated from a host, typically a human, including, but not limited to, plasma or serum. To confirm that a factor within donor plasma is immunologically cross-reactive with one or more epitopes of the disclosed peptides is a straightforward matter. This can be readily determined using specific assays, e.g., of a single proposed epitopic sequence, or using more general screens, e.g., of a pool of randomly generated synthetic peptides or protein fragments. The screening assays may be employed to identify-either equivalent antigens or cross-reactive antibodies. In any event, the principle is the same, i.e., based upon competition for binding sites between antibodies and antigens.

Detail Description Paragraph:
[0260] The objective of the studies described here was to determine if passive immunization with donor selected IVIG products prepared from human donor plasma containing high titers of antibodies against microbial surface components

recognizing adhesive matrix molecule (MSCRAMM) proteins expressed by Staphylococcus aureus (S. aureus) can prevent mortality caused by an antibiotic resistant S. aureus clinical isolate in a murine septicemia model.

Detail Description Paragraph:
[0277] Mice were treated by intraperitoneal (IP) injection with 20 mg of SA-IVIG MS502 either 18 or prior or 3 hours after an IV challenge with S. aureus 601. MS502 was an immunoglobulin G (IgG) preparation purified from donor plasma containing elevated titers of antibodies recognizing the A domain of clumping factor (ClfA), a S. aureus fibrinogen binding MSCRAMM protein. The mice were followed for 5 days at which point all remaining mice were sacrificed. Ninety-three percent of the mice that received MS502 SA-IVIG 18 hours prior to S. aureus challenge survived. Similarly, 93% of the mice that received MS502 SA-IVIG 3 hours post bacterial challenge survived. In contrast, only 76% of the control mice survived the bacterial challenge. These results clearly indicate that therapeutic administration of ClfA donor selected human SA-IVIG provides a significant and effective treatment of staphylococcal infection as compared to a commercially available normal human IVIG product.

CLAIMS:

5. The method according to claim 4 wherein the second adhesin is a staphylococcal Sdr protein.

6. The method according to claim 5 wherein donors having a high titer to the staphylococcal Sdr protein are determined by identifying those samples having a high titer of antibodies to the A domain of the staphylococcal Sdr protein.

7. The method according to claim 5 wherein the staphylococcal Sdr protein is selected from the group consisting of SdrF, SdrG, and SdrH.

8. The method according to claim 5 wherein the staphylococcal Sdr protein is SdrF.

9. The method according to claim 5 wherein the staphylococcal Sdr protein is SdrG.

10. The method according to claim 5 wherein the staphylococcal Sdr protein is SdrH.

16. The method according to claim 15 wherein the second adhesin is a staphylococcal Sdr protein.

17. The method according to claim 16 wherein the host donor is induced to have an antibody titer to the staphylococcal Sdr protein in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected donors by administering the A domain of the staphylococcal Sdr protein an amount sufficient so as to induce an antibody titer to the staphylococcal Sdr protein in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected donors.

18. The method according to claim 16 wherein the staphylococcal Sdr protein is selected from the group consisting of SdrF, SdrG, and SdrH.

19. The method according to claim 18 wherein the staphylococcal Sdr protein is SdrF.

20. The method according to claim 18 wherein the staphylococcal Sdr protein is SdrG.

21. The method according to claim 18 wherein the staphylococcal Sdr protein comprises SdrH.

23. A method of obtaining an immunoglobulin composition having a higher than normal antibody titer to a staphylococcal Sdr protein comprising obtaining blood or plasma samples from donors, identifying those blood or plasma samples from high-titer donors having the presence of an antibody titer to a staphylococcal Sdr protein in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected donors, recovering blood or plasma from the identified high-titer donors, and treating the donor blood or plasma to obtain immunoglobulin in a purified state that has an antibody titer to a staphylococcal Sdr protein in an amount which is higher than that found in intravenous immunoglobulin obtained from unselected donors.

24. The method according to claim 23 wherein donors are identified which have an antibody titer to a staphylococcal Sdr protein in an amount which is 2-fold or greater than that found in pooled intravenous immunoglobulin obtained from unselected donors.

25. The method according to claim 23 wherein donors having a high titer to a staphylococcal Sdr protein are determined by identifying those samples having a high titer of antibodies to the A domain of a staphylococcal Sdr protein.

27. The method according to claim 26 wherein the second adhesin is a second staphylococcal Sdr protein.

28. The method according to claim 27 wherein donors having a high titer to the second staphylococcal Sdr protein are determined by identifying those samples having a high titer of antibodies to the A domain of the second staphylococcal Sdr protein.

30. A method of obtaining an immunoglobulin composition having a higher than normal antibody titer to a staphylococcal Sdr protein comprising administering a staphylococcal Sdr protein to a host donor in an amount sufficient so as to induce an antibody titer to a staphylococcal Sdr protein in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected donors, recovering blood or plasma from the host donor, and treating the donor blood or plasma to obtain immunoglobulin in a purified state that has an antibody titer to a staphylococcal Sdr protein which is higher than that found in pooled intravenous immunoglobulin obtained from unselected donors.

31. The method according to claim 30 wherein the host donor is induced to have an antibody titer to a staphylococcal Sdr protein in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected donors by administering the A domain of a staphylococcal Sdr protein to the host donor in an amount sufficient so as to induce an antibody titer to a staphylococcal Sdr protein in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected donors.

32. The method according to claim 30 wherein immunoglobulin is obtained that has an antibody titer to a staphylococcal Sdr protein in an amount which is 2-fold or greater than that found in pooled intravenous immunoglobulin obtained from unselected donors.

34. The method according to claim 33 wherein the second adhesin is a second staphylococcal Sdr protein.

35. The method according to claim 34 wherein the host donor is induced to have an antibody titer to the second staphylococcal Sdr protein in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected donors by administering the A domain of the second staphylococcal Sdr protein an amount sufficient so as to induce an antibody titer to the second

staphylococcal Sdr protein in an amount which is higher than that found in pooled intravenous immunoglobulin obtained from unselected donors.

37. A method of immunizing patients so as to treat or prevent staphylococcal infection comprising administering an immunologically effective amount of the composition of claim 1 to a patient in need of said treatment.

40. The method according to claim 4 wherein the second adhesin is the A domain of a staphylococcal adhesin selected from the group consisting of proteins FnBP-A, FnBP-B, ClfB, SdrC, SdrD, SdrE, SdrF, SdrG, SdrH, CNA, EbpS and MHCII.

41. The method according to claim 30 wherein the staphylococcal Sdr protein is from a staphylococcal bacteria selected from the group consisting of Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, and Staphylococcus saprophyticus.

0008679952 BIOSIS NO.: 199345110940
Safety and immunogenicity of a %%%conjugate%%% vaccine against %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% capsular polysaccharide in hemodialysis (HD) patients
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JOURNAL: Journal of the American Society of Nephrology 4 (3): p259 1993
CONFERENCE/MEETING: 26th Annual Meeting of the ASN (American Society of Nephrology) Boston, Massachusetts, USA November 14-17, 1993; 19931114
ISSN: 1046-6673
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: English

0008807510 BIOSIS NO.: 199395109776

Laboratory and clinical evaluation of %%%conjugate%%% vaccines composed of %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% and %%%type%%% %%%8%%% capsular polysaccharides bound to Pseudomonas aeruginosa recombinant exoprotein A

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JOURNAL: Infection and Immunity 61 (3): p1023-1032 1993

ISSN: 0019-9567

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The synthesis, standardization, and immunogenicity in young outbred mice and clinical evaluation in adult volunteers of investigational vaccines designed to induce serum antibodies to the %%%type%%% %%%5%%% and %%%type%%% %%%8%%% capsular polysaccharides (CPs) of %%%Staphylococcus%%% aureus are described. %%%Conjugates%%% composed of the %%%type%%% %%%5%%% CP and a sonicated preparation of a high-molecular-weight %%%type%%% %%%8%%% CP bound to a nontoxic recombinant protein derived from Pseudomonas aeruginosa exotoxin A (rEPA) were synthesized. The %%%conjugates%%% were nontoxic and elicited serum CP antibodies after two subcutaneous injections into young outbred mice; a third injection elicited a booster response. The lower-molecular-weight %%%type%%% %%%8%%% CP was not immunogenic in the mice, and the high-molecular-weight %%%type%%% %%%8%%% CP elicited low levels of antibodies without a booster effect. In the volunteers, neither the %%%conjugates%%% nor the %%%type%%% %%%8%%% CP alone caused significant local reactions or fever. The %%%conjugates%%% elicited type-specific antibodies of both the immunoglobulin M (IgM) and IgG classes after the first injection; a second injection 6 weeks later did not stimulate a booster effect. The high-molecular-weight %%%type%%% %%%8%%% CP alone, injected once only, elicited levels of IgG and IgM type-specific antibodies similar to those of the %%%conjugate%%%. The vaccine-induced CP antibodies were mostly of the IgG1 and IgG2 subclasses and had opsonophagocytic activity. The %%%conjugates%%% elicited IgG antibodies to the native exotoxin A with neutralizing activity. In summary, the %%%type%%% %%%5%%% and %%%type%%% %%%8%%% %%%conjugates%%% were safe and elicited biologically active antibodies to both the CP and rEPA components.

0010130787 BIOSIS NO.: 199698598620
Effect of %%%conjugation%%% methodology, carrier protein, and adjuvants on the immune response to %%%Staphylococcus%%% aureus capsular polysaccharides
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JOURNAL: Vaccine 13 (14): p1288-1293 1995 1995
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Conjugate%%% vaccines were prepared with S. aureus %%%type%%% %%%8%%% capsular polysaccharide (CP) using three carrier proteins: Pseudomonas aeruginosa exotoxin A (ETA), a non-toxic recombinant ETA (rEPA), and diphtheria toxoid (DTd). Adipic acid dihydrazide (ADH) or N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) was used as a spacer to link the CP to carrier protein. All %%%conjugates%%% gave a high immune response with a boost after the second immunization. %%%Conjugates%%% prepared with ADH gave higher antibody titers than %%%conjugates%%% prepared with SPDP. IgG, was the primary subclass elicited by all %%%conjugates%%% regardless of the carrier protein or the %%%conjugation%%% method used to prepare the vaccines. The non-immunogenic CP and the %%%conjugates%%% were formulated with either monophosphoryl lipid A (MPL), QS21, or in Novasomes and evaluated in mice. While the adjuvants failed to improve the immunogenicity of the nonconjugated CP, a more than fivefold increase in the antibody levels was observed when these adjuvants were used with the %%%conjugates%%%. Significant rises in IgG-2b and IgG-3 were observed with all formulations. The enhancement of the immunogenicity and the IgG subclass shift, as seen with some adjuvants, mail, prove to be important in immunocompromised patients.

0010276254 BIOSIS NO.: 199698744087
Safety and immunogenicity of %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% capsular polysaccharide-Pseudomonas aeruginosa recombinant exoprotein A %%%conjugate%%% vaccine in patients on hemodialysis
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JOURNAL: Journal of the American Society of Nephrology 7 (2): p247-253 1996 1996
ISSN: 1046-6673
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Seventeen volunteers with ESRD on hemodialysis, negative for infection with HIV or hepatitis B and C and not receiving immunosuppressive therapy, were injected two times 6 wk apart with 25 mu-g of %%%Staphylococcus%%% aureus %%%Type%%% %%%5%%% capsular polysaccharide-Pseudomonas aeruginosa exoprotein A (rEPA) %%%conjugate%%% . Controls were healthy adults, 18 to 44 yr old, injected previously with the same vaccine. None of the patients had fever or significant elevations in their SGOT or SGPT attributable to the vaccine. Two vaccinees had transient induration gt 1 cm in diameter at the injection site. The preimmunization geometric mean (GM) %%%Type%%% %%%5%%% antibody levels of the ESRD patients and controls were similar. %%%Type%%% %%%5%%% antibody levels of the three major immunoglobulin (1g) classes rose at 2 and 6 wk after immunization (P lt 0.001 for IgG, P lt 0.005 for IgM, and P = 0.0001 for IgA). Reimmunization at 6 wk did not elicit a booster response. At 6 months, the GM IgG level of the patients was approximately 50% of that of the healthy volunteers and 14 of 17 had a more than fourfold higher antibody level than the preimmune value. The GM IgM level, in contrast, declined to the preimmunization value. Vaccine-induced %%%Type%%% %%%5%%% antibodies had opsonophagocytic activity. There was a slight increase of IgG antibodies to the heterologous S. aureus %%%Type%%% %%%8%%% polysaccharide (P lt 0.01) that was sustained at 6 months. The S. aureus %%%Type%%% %%%5%%%-rEPA vaccine is safe and immunogenic in ESRD patients, and evaluation of its effectiveness against S. aureus bacteremia in this at-risk group is planned.

0010356694 BIOSIS NO.: 199698824527
A %%%Staphylococcus%%% aureus capsular polysaccharide (CP) vaccine and CP-specific antibodies protect mice against bacterial challenge
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JOURNAL: Infection and Immunity 64 (5): p1659-1665 1996 1996
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The efficacy of capsular polysaccharide (CP)-specific antibodies elicited by active immunization with vaccines composed of %%%Staphylococcus%%% aureus types 5 and 8 CP linked to Pseudomonas aeruginosa exoprotein A or with immune immunoglobulin G (I-IgG) obtained from vaccinated plasma donors was tested in lethal and sublethal bacterial mouse challenge models. A dose of 2 times 10-5 CFU of S. aureus %%%type%%% %%%5%%% CP per mouse administered intraperitoneally (i.p.) with 5% hog mucin was found to cause 80 to 100% mortality in BALB/c mice within 2 to 5 days. Mice passively immunized i.p. 24 h earlier or subcutaneously 48 h earlier with 0.5 ml of I-IgG showed significantly higher average survival rates than animals receiving standard IgG or saline (P lt 0.01) following the bacterial challenge. Animals actively immunized with the monovalent %%%type%%% %%%5%%% CP-P. aeruginosa exoprotein A %%%conjugate%%% showed a survival rate of 73% compared with 13% in phosphate-buffered saline-immunized animals. The prechallenge geometric mean titer of %%%type%%% %%%5%%% CP antibodies in animals that died was significantly (P lt 0.05) lower than that of animals which survived the challenge (95.7 versus 223.6 mu-g/ml, respectively). The IgG was further evaluated in mice challenged i.p. with a sublethal dose of 5 times 10-4 CFU per mouse. Serial blood counts were performed on surviving animals at 6, 12, 24, and 48 h. Surviving animals were sacrificed at 72 h, and bacterial counts were performed on their kidneys, livers, and peritoneal lavage fluids. Animals receiving I-IgG had lower bacterial counts in blood samples and lower bacterial densities in kidneys, livers, and peritoneal lavage samples than mice immunized with standard IgG (P lt 0.05). These data suggest that S. aureus %%%type%%% %%%5%%% CP antibodies induced by active immunization or administered by passive immunization confer protection against S. aureus infections.

0011157144 BIOSIS NO.: 199799791204
Protective efficacy of antibodies to the %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% capsular polysaccharide in a modified model of endocarditis in rats
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JOURNAL: Infection and Immunity 65 (10): p4146-4151 1997 1997
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The protective efficacy of antibodies to the %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% capsular polysaccharide (CP5) was examined in a modified model of catheter-induced endocarditis. Rats were catheterized by surgically passing a polyethylene catheter through the right carotid artery and aortic valve into the left ventricle. The following day, the rats were injected by the intraperitoneal (i.p.) route with immunoglobulin G (IgG) purified from nonimmunized rabbits or from rabbits immunized with a %%%conjugate%%% vaccine composed of CP5 and CP8 linked covalently to recombinant Pseudomonas aeruginosa exotoxoid A. One day after passive immunization, the animals were challenged i.p. with one of three serotype 5 S. aureus isolates (strain Reynolds, Lowenstein, or VP) or nontypeable strain 521. Protection was evaluated by comparing quantitative cultures of blood, endocardial vegetations, and kidneys from control and immune animals. For experiments performed with S. aureus Reynolds and Lowenstein, rats given capsular antibodies (645 mu-g of CP5-specific IgG) showed a significantly (P lt 0.05) lower prevalence of endocarditis than rats injected with nonimmune IgG. Similarly, quantitative cultures of the blood, kidneys, and aortic valve vegetations revealed that fewer S. aureus cells were recovered from rats given capsule-specific IgG than from rats administered nonimmune IgG. Rats challenged with strain VP were protected with 1.145 mg of CP5-specific IgG. Capsular antibodies did not protect against infection elicited by a nontypeable strain. These results demonstrate that capsular antibodies elicited by immunization with a polysaccharide-protein %%%conjugate%%% vaccine protect experimental animals against serotype 5 S. aureus infection in a modified model of endocarditis.

0011686347 BIOSIS NO.: 199800480594
Antigenic determinants of %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% and %%%type%%% %%%8%%% capsular polysaccharide vaccines
AUTHOR: Fattom Ali I (Reprint); Sarwar Jawad; Basham Lisa; Ennifar Sofiane; Naso Robert
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JOURNAL: Infection and Immunity 66 (10): p4588-4592 Oct., 1998 1998
MEDIUM: print
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Bacterial capsular polysaccharides (CP) are carbohydrate polymers comprised of repeating saccharide units. Several of these CP have side chains attached to their backbone structures. The side chains may include O-acetyl, phosphate, sialic acid, and other moieties. Those moieties represent the immunodominant epitopes and the most functional ones. The clinically significant %%%Staphylococcus%%% aureus %%%type%%% %%%5%%% CP (CP 5) and %%%type%%% %%%8%%% CP (CP 8) are comprised of a trisaccharide repeat unit with one O-acetyl group attached to each repeat unit. The immunogenicity of these CP and the functionality of antibodies to the backbone and the O-acetyl moieties were investigated. Immunization with the native CP %%%conjugates%%% (CP with 75% O-acetylation) elicited a high proportion of antibodies directed against the O-acetyl moiety. Nonetheless, all of the vaccines produced antibodies to the backbone moieties as well. %%%Conjugate%%% vaccines made of de-O-acetylated CP elicited backbone antibodies only. Antibodies to both backbone and O-acetyl groups were found to be opsonic against S. aureus strains which varied in their O-acetyl content. Absorption studies with O-acetylated and de-O-acetylated CP showed that (i) native CP %%%conjugates%%% generated antibodies to both backbone and O-acetyl groups and (ii) O-acetylated isolates were opsonized by both populations of antibodies while the non-O-acetylated strains were predominantly opsonized by the backbone antibodies. These results suggest that S. aureus CP %%%conjugate%%% vaccines elicit multiple populations of antibodies with diverse specificities. Moreover, the antibodies of different specificities (backbone or O-acetyl) are all functional and efficient against the variations in bacterial CP that may occur among clinically significant S. aureus pathogenic isolates.

0012907108 BIOSIS NO.: 200100078947
Prevalence of capsular polysaccharide (CP) types of %%%Staphylococcus%%% aureus isolated from bovine mastitic milk and protection of S. aureus infection in mice with CP vaccine
AUTHOR: Han Hong Ryul; Pak Son Il (Reprint); Guidry Albert
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JOURNAL: Journal of Veterinary Medical Science 62 (12): p1331-1333 December, 2000 2000
MEDIUM: print
ISSN: 0916-7250
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: To determine the prevalence of capsular polysaccharide (CP) types of %%%Staphylococcus%%% aureus isolated from bovine mastitic milk in Korea, the protective effect of the %%%conjugates%%%, composed of microencapsulated S. aureus clinical isolate %%%type%%% %%%8%%% CP bound to Pseudomonas aeruginosa exotoxin A (ETA) was evaluated in mice. Of 107 S. aureus isolates, serotype 5 and 8 accounted for only 26 or 24.2%. When serotype 336 antiserum was employed, fifty of the remaining 81 isolates were typed as 336, 26 reacted with two serotypes, and 5 were nontypeable. Mice challenged with the same strain used for immunization had fewer S. aureus cells in their kidneys than mice challenged with the heterologous strain. But the magnitudes of difference on bacterial clearance were similar in both groups, indicating that the significance of this result remains to be determined. Mice immunized with the %%%conjugate%%% elicited an antibody response 3 days post injection, which persisted for 13 days of the observation period after second injection in some mice. The mice immunized with the CP8-ETA %%%conjugates%%% developed antibodies significantly higher than those immunized with CP-Freund's adjuvant or PBS. In in vivo bacterial challenge experiment, the survival rate of mice immunized with CP8-ETA %%%conjugate%%% was significantly higher than that of mice immunized with PBS. It was suggested that CP8-ETA vaccine had a potential to protect mice against experimental S. aureus bacteremia.

7/7/132 (Item 8 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00118366

Medical Progress: %%%Staphylococcus%%% aureus Infections (Review Articles)

Lowy, Franklin D.
The New England Journal of Medicine
Aug 20, 1998; 339 (8),pp 520-532
LINE COUNT: 00701 WORD COUNT: 09682
ISSN: 0028-4793
CORPORATE SOURCE: From the Division of Infectious Diseases, Department of Medicine, Montefiore Medical Center, and the Departments of Medicine, Microbiology, and Immunology, Albert Einstein College of Medicine -- both in Bronx, N.Y. Address reprint requests to Dr. Lowy at the Department of Medicine, Montefiore Medical Center, 111 E. 210th St., Bronx, NY 10467.||Micrococcus, which, when limited in its extent and activity, causes acute suppurative inflammation (phlegmon), produces, when more extensive and intense in its action on the human system, the most virulent forms of septicaemia and pyaemia. *RF 1*

03885578 NLM Doc No: CRISP/96/HD01301-13 Sec. Source ID: CRISP/96/HD01301-13

HUMAN IMMUNE RESPONSE TO %%%POLYSACCHARIDE%%%-PROTEIN CONJUGATE %%%VACCINES%%%

SCHNEERSON R
NICHD, NIH

Source: Crisp Data Base National Institutes Of Health
Pub. Year: 1995
Sponsoring Agency: U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
Award Type: Intramural Project
Document type: Research
Languages: ENGLISH
Record type: Completed

RPROJ The surface %%%polysaccharides%%% of bacterial pathogens, which include capsular %%%polysaccharides%%% and lipopolysaccharides, serve as protective antigens. The immunologic properties of these bacterial %%%polysaccharides%%% , namely their age-related and T-cell independent immunogenicity, limit their use as %%%vaccines%%%. Covalently attachment to medically-useful proteins to form conjugates, both increases their immunogenicity and confers T-cell dependent properties to these %%%polysaccharides%%%. The capsular %%%polysaccharides%%% of Streptococcus pneumococcus type 6B, %%%Staphylococcus%%% aureus types 5 and 8, Group B streptococcus type 3 have been bound to several proteins and evaluated clinically. S. aureus type 5-rEPA was evaluated in end stage %%%renal%%% disease patients; type 5 antibodies of the three major Ig classes rose significantly though to a lesser degree than in healthy volunteers, no booster response to reinjection at 6 weeks was found. These antibodies had opsonophagocytic activities. Pn6B-TT was evaluated in patients with sickle cell disease, healthy infants at 3, 4 and 6 months of age or at 7 and 9 months of age. Type specific antibodies of the three Ig classes, with booster responses, were induced. The magnitude of these responses was lesser than of Hib- TT. GBSIII-TT was evaluated in females of child bearing age. IgG antitype III rose similarly to the response to the %%%polysaccharide%%% alone. Technical problems with this lot were identified. All conjugates were safe, with only minor local reaction. The LPS of shigellae was detoxified, their O-specific %%%polysaccharides%%% bound to bacterial toxoids and their immunogennicity in mice found to be satisfactory. In Phase 1 and Phase 2 studies, these conjugates of the O-specific %%%polysaccharides%%% were safe and immunogenic: LPS antibody levels elicited by the investigational conjugates were similar to those in recruits convalescent from shigellosis. In preliminary studies, a S. sonnei-rEPA conjugate protected against shigellosis caused by this pathogen. A more extensive study showed protection of 75%.

Record Date Created: 199604

15884949 PMID: 15040941

Development of StaphVAX trade mark, a %%%polysaccharide%%% conjugate %%%vaccine%%% against S. aureus infection: from the lab bench to phase III clinical trials.

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Vaccine (Netherlands) Feb 17 2004, 22 (7) p880-7, ISSN 0264-410X
Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Data Review

%%%Staphylococcus%%% aureus is the most common nosocomial pathogen and is responsible for approximately one-third of hospital-acquired bacteremias. The emergence of strains with multidrug resistance, including resistance to vancomycin, the antibiotic of last resort, presents the medical community with a major public health problem. Alternative therapies, including immunotherapy, have been in development for several decades. The discovery of S. aureus capsular %%%polysaccharides%%% from clinical isolates, and their importance to pathogenicity via antiphagocytic activity, opened a new window of opportunity for development of %%%vaccines%%% and immunotherapy against this pathogen. A conjugate %%%vaccine%%%, StaphVAX trade mark that includes the two most prevalent capsular %%%polysaccharides%%%, types 5 and 8, coupled to a carrier protein efficient in promoting a Th2 response, was developed. In a recent phase III clinical study in %%%hemodialysis%%% patients, StaphVAX trade mark was shown to prevent S. aureus bacteremia for up to 10 months following a single immunization. The history, epidemiology, serology, and development of StaphVAX trade mark, including preclinical and clinical studies demonstrating efficacy are described in this review.

Record Date Created: 20040325

In December 1987, a new %%%vaccine%%% - known as a conjugate %%%vaccine%%%, a technical reference to a new method of formulation - was licensed by FDA for children 18 months of age or older, in whom it was clearly more effective than the %%%polysaccharide%%% %%%vaccines%%%; one year later, a second conjugate %%%vaccine%%% was licensed for the same age group.

A third such %%%vaccine%%% was licensed in December 1989, with the statement that it could be administered to children as young as 15 months. The following spring, ACIP revised its recommendations, advising routine immunization of all children at the age of 15 months, using any of the three conjugate %%%vaccines%%%.

Late in 1990, after further clinical testing, FDA announced approval of two of the three %%%vaccines%%% for babies as young as 2 months of age. This was especially good news, since about two-thirds of all cases of Hib disease have struck children under the age of 15 months.

%%%Vaccination%%% against Hib infection is now considered part of the routine childhood immunization schedule, and is accomplished with the following conjugate %%%vaccines%%%:

* HbOC (HibTITER), made by Praxis Biologics, distributed by Lederle Laboratories
* PRP-OMP (PedvaxHIB), made by Merck Sharp & Dohme
* PRP-D (ProHIBit), made by Connaught Laboratories, only for children at least 15 months old.

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? ds

Set      Items   Description
S1         762   (TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
S2         295   RD S1 (unique items)
S3         680   STAPHYLOCOCC? AND VACCIN? AND POLYSACCHARIDE?
S4         452   RD S3 (unique items)
S5      833359   4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOSU-
              PPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSPL-
              ANT OR SURICAL OR BURN)
S6         140   S4 AND (IMMUNOCOMPROM? OR RENAL OR HEMODIALYSIS OR IMMUNOS-
              UPPRESS? OR AIDS OR DIABETIC OR NEONATES OR ELDERLY OR TRANSP-
              LANT OR SURICAL OR BURN)
S7         140   RD S6 (unique items)
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? ds

Set      Items    Description
S1         748    (TYPE(W)5 OR TYPE(W)8) AND STAPHYLOCOCC?
S2         262    RD S1 (unique items)
S3          28    S2 AND CONJUGAT?
S4          53    S2 AND VACCIN?
? ds
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